

**WEST****Freeform Search****Database:**

US Patents Full-Text Database	▲
US Pre-Grant Publication Full-Text Database	
JPO Abstracts Database	▼
EPO Abstracts Database	
Derwent World Patents Index	
IBM Technical Disclosure Bulletins	▼

**Term:**

	▲
	▼

**Display:**  **Documents in Display Format:**  **Starting with Number** **Generate:**  Hit List  Hit Count  Image

---

Search	Clear	Help	Logout	Interrupt
--------	-------	------	--------	-----------

---

Main Menu	Show S Numbers	Edit S Numbers	Preferences
-----------	----------------	----------------	-------------

---

**Search History**

---

**Today's Date:** 12/5/2001

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
JPAB,EPAB,DWPI	superoxide dismutase or sod	2510	<u>L1</u>
JPAB,EPAB,DWPI	(copper zinc) or (cu zn)or cuprozinc or cuzn or cu/zn	12393	<u>L2</u>
JPAB,EPAB,DWPI	11 with 12 or cuznsod	196	<u>L3</u>
JPAB,EPAB,DWPI	vaccine or vaccinat\$	20130	<u>L4</u>
JPAB,EPAB,DWPI	immunis\$ or immuniz\$	9324	<u>L5</u>
JPAB,EPAB,DWPI	13 and 14	5	<u>L6</u>
JPAB,EPAB,DWPI	13 and 15	10	<u>L7</u>
JPAB,EPAB,DWPI	11 near3 human	258	<u>L8</u>
JPAB,EPAB,DWPI	17 not 18	3	<u>L9</u>
JPAB,EPAB,DWPI	bacteri\$ or gram negative	112306	<u>L10</u>
JPAB,EPAB,DWPI	110 with 13	17	<u>L11</u>
JPAB,EPAB,DWPI	111 and (14 or 15)	2	<u>L12</u>
JPAB,EPAB,DWPI	112 not 16	0	<u>L13</u>
JPAB,EPAB,DWPI	13 and 110 and (14 or 15)	2	<u>L14</u>
JPAB,EPAB,DWPI	114 not 112	0	<u>L15</u>
JPAB,EPAB,DWPI	meningococc\$ or meningitis or actinobacillus or pleuropneumoniae or pasteurellaceae or neisseria or haemophilus or salmonella or salmonellosis or escherichia	12277	<u>L16</u>
JPAB,EPAB,DWPI	13 and 116	13	<u>L17</u>
JPAB,EPAB,DWPI	117 and (14 or 15)	2	<u>L18</u>
JPAB,EPAB,DWPI	118 not 112	0	<u>L19</u>
JPAB,EPAB,DWPI	17 or 111	27	<u>L20</u>
JPAB,EPAB,DWPI	120 not (16 or 19 or 112)	21	<u>L21</u>

**WEST****Generate Collection****Search Results - Record(s) 1 through 5 of 5 returned.** **1. Document ID: US 5188936 A**

L6: Entry 1 of 5

File: EPAB

Feb 23, 1993

PUB-NO: US005188936A

DOCUMENT-IDENTIFIER: US 5188936 A

TITLE: Brucella abortus antibody detection methods

PUBN-DATE: February 23, 1993

## INVENTOR-INFORMATION:

NAME	COUNTRY
TABATABAI, LOUISA B	US
MAYFIELD, JOHN E	US
BECK, BONNIE L	US

INT-CL (IPC): C12N 15/53; G01N 33/569

EUR-CL (EPC): G01N033/569; G01N033/573

## ABSTRACT:

Diagnostic reagents comprising the 20 kd Brucella abortus CuZn superoxide dismutase (B. abortus lCuZnSOD) protein and peptide segments thereof, which are effective as antigenic determinants, have been identified. These reagents are useful for detecting an antibody response to the B. abortus CuZnSOD protein in bovine serum or other body fluid samples and can also be used for distinguishing between animals which have serum antibody of a natural B. abortus infection and those which have an antibody response to a B. abortus Strain 19 vaccine or a B. abortus Strain which does not express the 20 kd protein.

L6: Entry 1 of 5

File: EPAB

Feb 23, 1993

DOCUMENT-IDENTIFIER: US 5188936 A

TITLE: Brucella abortus antibody detection methods

## FPAR:

Diagnostic reagents comprising the 20 kd Brucella abortus CuZn superoxide dismutase (B. abortus lCuZnSOD) protein and peptide segments thereof, which are effective as antigenic determinants, have been identified. These reagents are useful for detecting an antibody response to the B. abortus CuZnSOD protein in bovine serum or other body fluid samples and can also be used for distinguishing between animals which have serum antibody of a natural B. abortus infection and those which have an antibody response to a B. abortus Strain 19 vaccine or a B. abortus Strain which does not express the 20 kd protein.

2. Document ID: EP 1126874 A2, WO 200025811 A2, AU 200010569 A, BR 9914946 A

L6: Entry 2 of 5

File: DWPI

Aug 29, 2001

DERWENT-ACC-NO: 2000-365400

DERWENT-WEEK: 200150

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Compositions for conferring protective immunity to Gram negative bacteria, especially *Neisseria meningitidis*, the causal agent of meningococcal meningitis, comprise both transferrin binding proteins A and B

INVENTOR: GORRINGE, A R; HUDSON, M J ; REDDIN, K M ; ROBINSON, A

PRIORITY-DATA: 1998GB-0023978 (November 2, 1998)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1126874 A2	August 29, 2001	E	000	A61K039/095
WO 200025811 A2	May 11, 2000	E	026	A61K039/00
AU 200010569 A	May 22, 2000		000	A61K039/00.
BR 9914946 A	July 10, 2001		000	A61K039/00

INT-CL (IPC): A61K 39/00; A61K 39/095; A61P 31/04; C07K 14/22; A61K 38/44; A61K 39/095

ABSTRACTED-PUB-NO: WO 200025811A

## BASIC-ABSTRACT:

NOVELTY - Compositions which confer improved protective immunity to Gram negative bacteria comprise both transferrin binding proteins (Tbps) A and B, or Tbps and other components.

## DETAILED DESCRIPTION - The compositions may comprise:

- (i) transferrin binding proteins A (TbpA) and B (TbpB);
- (ii) a complex of two TbpAs and one TbpB;
- (iii) TbpA and/or TbpB and *N. meningitidis* outer membrane vesicles; or (iv) TbpA and/or TbpB and a Cu, Zn-superoxide dismutase (Cu, Zn-SOD).

## INDEPENDENT CLAIMS are also included for the following:

- (1) a vaccine comprising a composition as above;
- (2) a method of manufacturing the composition comprising combining a covalently linked complex of TbpA and TbpB with *N. meningitidis* outer membrane vesicles and a pharmaceutically acceptable carrier;
- (3) a method of manufacturing a composition comprising combining a covalently linked complex of TbpA and TbpB with a Cu, Zn-SOD and a pharmaceutically acceptable carrier.

USE - The compositions (especially (i); claimed) are useful to treat Gram negative bacterial infections, especially with *Neisseria meningitidis*, the causal agent of meningococcal meningitis. They (especially (i); claimed) can be used to produce vaccines which can be administered to confer protective immunity to infection or protect against sub-clinical infection (i.e. where symptoms are not immediately apparent) with Gram negative bacteria; the vaccines are particularly useful to provide immunity to a broad spectrum of *N. meningitidis* strains simultaneously to protect against meningococcal disease.

ADVANTAGE - Compositions comprising TbpA plus TbpB provided higher protective immunity to meningococcal infection than prior art compositions comprising TbpB alone. The compositions of (iii) can also provide more effective and/or broader spectrum protection against N. meningitidis than existing vaccines, since they present a wider combination of N. meningitidis antigens, and the Tbps are presented in a highly antigenic environment that closely mimics that on live, infecting bacteria. Similarly, the compositions of (iv) additionally comprise Cu,Zn-SOD, which has previously been identified in the periplasm of Gram negative species, including N. meningitidis.

L6: Entry 2 of 5

File: DWPI

Aug 29, 2001

DERWENT-ACC-NO: 2000-365400

DERWENT-WEEK: 200150

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Compositions for conferring protective immunity to Gram negative bacteria, especially Neisseria meningitidis, the causal agent of meningococcal meningitis, comprise both transferrin binding proteins A and B

ABTX:

(iii) TbpA and/or TbpB and N. meningitidis outer membrane vesicles; or (iv) TbpA and/or TbpB and a Cu,Zn-superoxide dismutase (Cu,Zn-SOD).

ABTX:

(1) a vaccine comprising a composition as above;

ABTX:

(3) a method of manufacturing a composition comprising combining a covalently linked complex of TbpA and TbpB with a Cu, Zn-SOD and a pharmaceutically acceptable carrier.

ABTX:

USE - The compositions (especially (i); claimed) are useful to treat Gram negative bacterial infections, especially with Neisseria meningitidis, the causal agent of meningococcal meningitis. They (especially (i); claimed) can be used to produce vaccines which can be administered to confer protective immunity to infection or protect against sub-clinical infection (i.e. where symptoms are not immediately apparent) with Gram negative bacteria; the vaccines are particularly useful to provide immunity to a broad spectrum of N. meningitidis strains simultaneously to protect against meningococcal disease.

ABTX:

ADVANTAGE - Compositions comprising TbpA plus TbpB provided higher protective immunity to meningococcal infection than prior art compositions comprising TbpB alone. The compositions of (iii) can also provide more effective and/or broader spectrum protection against N. meningitidis than existing vaccines, since they present a wider combination of N. meningitidis antigens, and the Tbps are presented in a highly antigenic environment that closely mimics that on live, infecting bacteria. Similarly, the compositions of (iv) additionally comprise Cu,Zn-SOD, which has previously been identified in the periplasm of Gram negative species, including N. meningitidis.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)[KWC](#) | [Drawn Desc](#) | [Image](#)

3. Document ID: EP 1108038 A1, WO 200012718 A1, AU 9956350 A

L6: Entry 3 of 5

File: DWPI

Jun 20, 2001

DERWENT-ACC-NO: 2000-237879

DERWENT-WEEK: 200135

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Vaccine for providing protection against bacterial infection, particularly meningococcal infection, comprises a copper, zinc-superoxide dismutase of the dimeric type

INVENTOR: GORRINGE, A R; KROLL, J S ; LANGFORD, P R ; ROBINSON, A

PRIORITY-DATA: 1998GB-0018756 (August 27, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 1108038 A1	June 20, 2001	E	000	C12N015/53
WO 200012718 A1	March 9, 2000	E	027	C12N015/53
AU 9956350 A	March 21, 2000		000	C12N015/53

INT-CL (IPC): A61K 31/70; A61K 38/44; A61K 48/00; C07K 16/40; C12N 9/02; C12N 15/53

ABSTRACTED-PUB-NO: WO 200012718A

BASIC-ABSTRACT:

NOVELTY - A vaccine (I) comprising a copper, zinc-superoxide dismutase (Cu,Zn-SOD) of the dimeric type, a fragment, variant or derivative, or a nucleic acid coding Cu,Zn-SOD, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method of preparing a pharmaceutical composition comprising:

(a) cloning a gene for a Cu,Zn-SOD of the dimeric type to obtain a recombinant form of the gene; and

(b) synthesizing Cu,Zn-SOD from the recombinant gene;

(2) a pharmaceutical preparation comprising an antibody to a Cu,Zn-SOD as above;

(3) a multivalent vaccine (II) comprising many Cu,Zn-SODs from the same or different species of Gram negative bacteria; and

(4) an antibody specific to bacterial Cu,Zn-SOD.

ACTIVITY - Bacteriocidal; immunostimulatory.

No biological data.

MECHANISM OF ACTION - Vaccine.

USE - The vaccine is useful for providing protection against bacterial infection, particularly gram negative bacteria, especially meningococcal infection.

L6: Entry 3 of 5

File: DWPI

Jun 20, 2001

DERWENT-ACC-NO: 2000-237879

DERWENT-WEEK: 200135

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Vaccine for providing protection against bacterial infection, particularly meningococcal infection, comprises a copper, zinc-superoxide dismutase of the dimeric type

ABTX:

NOVELTY - A vaccine (I) comprising a copper, zinc-superoxide dismutase (Cu, Zn-SOD) of the dimeric type, a fragment, variant or derivative, or a nucleic acid coding Cu, Zn-SOD, is new.

ABTX:

(a) cloning a gene for a Cu, Zn-SOD of the dimeric type to obtain a recombinant form of the gene; and

ABTX:

(b) synthesizing Cu, Zn-SOD from the recombinant gene;

ABTX:

(2) a pharmaceutical preparation comprising an antibody to a Cu, Zn-SOD as above;

ABTX:

(3) a multivalent vaccine (II) comprising many Cu, Zn-SODs from the same or different species of Gram negative bacteria; and

ABTX:

(4) an antibody specific to bacterial Cu, Zn-SOD.

ABTX:

MECHANISM OF ACTION - Vaccine.

ABTX:

USE - The vaccine is useful for providing protection against bacterial infection, particularly gram negative bacteria, especially meningococcal infection.

TTX:

VACCINE PROTECT BACTERIA INFECT MENINGOCOCCUS INFECT COMPRISE COPPER ZINC DISMUTASE DIMERISE TYPE

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMD](#) | [Draw Desc](#) | [Image](#)

---

4. Document ID: JP 05184359 A

L6: Entry 4 of 5

File: DWPI

Jul 27, 1993

DERWENT-ACC-NO: 1993-269029

DERWENT-WEEK: 199334

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Anti SOD monoclonal antibody and hybridoma producing it - comprises using spleen cells fused with mouse myeloma cells

PRIORITY-DATA: 1983GB-0030981 (November 21, 1983), 1983GB-0026508 (October 4, 1983)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 05184359 A	July 27, 1993		005	C12N005/20

INT-CL (IPC): A61K 39/395; C12N 5/20; C12N 15/06; C12P 21/08; C12P 21/08; C12R 1/91

ABSTRACTED-PUB-NO: JP05184359A

BASIC-ABSTRACT:

An anti SOD monoclonal antibody and a hybridoma producing it are new.

Prepn. of an anti-Cu, Zn-SOD monoclonal antibody. (I) Prepn. of immunised spleen cells. Cu, Zn-SOD was prep'd. from human red blood cells, and dissolved in a phosphate buffered saline (PBS) at concn. 1 mg/ml. The 100 micro-litres soln. was administered to female BALB/c mouse with 100 micro-grams mixt. of diphtheria.tetanus toxoid-pertussis vaccine, intraperitoneally. After 28 days, further 100 micro-litres of Cu, Zn-SOD soln. was administered intravenously. Then, after 4 days, the mouse was sacrificed, and spleen cells were collected. (II) Prepn. of hybridoma. The spleen cells were fused with mouse myeloma cells P3X63Ag8U1 by Kohler and Milstein methods. (III) Assay of anti-Cu, Zn-SOD antibody. (IV) Cloning of an anti-Cu, Zn-SOD antibody producing hybridoma, and (V) Identification of the antibody's immunoglobulin class were proceeded.

USE/ADVANTAGE - Specific anti SOD antibody with high yield can be prep'd. Also a large amt. of desired anti SOD antibody can be offered easil

L6: Entry 4 of 5

File: DWPI

Jul 27, 1993

DERWENT-ACC-NO: 1993-269029

DERWENT-WEEK: 199334

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Anti SOD monoclonal antibody and hybridoma producing it - comprises using spleen cells fused with mouse myeloma cells

ABTX:

Prepn. of an anti-Cu, Zn-SOD monoclonal antibody. (I) Prepn. of immunised spleen cells. Cu, Zn-SOD was prep'd. from human red blood cells, and dissolved in a phosphate buffered saline (PBS) at concn. 1 mg/ml. The 100 micro-litres soln. was administered to female BALB/c mouse with 100 micro-grams mixt. of diphtheria.tetanus toxoid-pertussis vaccine, intraperitoneally. After 28 days, further 100 micro-litres of Cu, Zn-SOD soln. was administered intravenously. Then, after 4 days, the mouse was sacrificed, and spleen cells were collected. (II) Prepn. of hybridoma. The spleen cells were fused with mouse myeloma cells P3X63Ag8U1 by Kohler and Milstein methods. (III) Assay of anti-Cu, Zn-SOD antibody. (IV) Cloning of an anti-Cu, Zn-SOD antibody producing hybridoma, and (V) Identification of the antibody's immunoglobulin class were proceeded.

5. Document ID: US 5188936 A

L6: Entry 5 of 5

File: DWPI

Feb 23, 1993

DERWENT-ACC-NO: 1993-085536

DERWENT-WEEK: 199310

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Detection of *Brucella abortus* antibody - using *B. abortus* copper-zinc superoxidizedismutase protein or segments contg. antigenic determinants

INVENTOR: BECK, B L; MAYFIELD, J E ; TABATABAI, L B

PRIORITY-DATA: 1991US-0641346 (January 16, 1991)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5188936 A	February 23, 1993		012	G01N033/569

INT-CL (IPC): C12N 15/53; G01N 33/569

ABSTRACTED-PUB-NO: US 5188936A

## BASIC-ABSTRACT:

A method is claimed for detecting an antibody elicited in response to the presence of *Brucella abortus* contg. *B. abortus* copper-zinc superoxide dismutase (CuZnSOD). The method comprises combining a diagnostic reagent comprising a pure *B. abortus* CuZn SOD protein or a segment of such protein effective as an antigenic determinant, with a body fluid sample suspected of contg. the antibody and detecting the presence of a complex of the reagent and the antibody.

USE - The method can be used for detecting *B. abortus* infection in animals, in partic. bovine brucellosis. The method can distinguish between animals which have a natural infection and those which have been vaccinated.

L6: Entry 5 of 5

File: DWPI

Feb 23, 1993

DERWENT-ACC-NO: 1993-085536

DERWENT-WEEK: 199310

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Detection of *Brucella abortus* antibody - using *B. abortus* copper-zinc superoxidizedismutase protein or segments contg. antigenic determinants

## ABTX:

A method is claimed for detecting an antibody elicited in response to the presence of *Brucella abortus* contg. *B. abortus* copper-zinc superoxide dismutase (CuZnSOD). The method comprises combining a diagnostic reagent comprising a pure *B. abortus* CuZn SOD protein or a segment of such protein effective as an antigenic determinant, with a body fluid sample suspected of contg. the antibody and detecting the presence of a complex of the reagent and the antibody.

## ABTX:

USE - The method can be used for detecting *B. abortus* infection in animals, in partic. bovine brucellosis. The method can distinguish between animals which have a natural infection and those which have been vaccinated.

Term	Documents
(3 AND 4).JPAB,EPAB,DWPI.	5

Documents, starting with Document:

**Display Format:**

**WEST****Generate Collection****Search Results - Record(s) 1 through 3 of 3 returned.** **1. Document ID: JP 01280255 A**

L9: Entry 1 of 3

File: JPAB

Nov 10, 1989

PUB-NO: JP401280255A  
DOCUMENT-IDENTIFIER: JP 01280255 A  
TITLE: INSPECTION OF RENAL INSUFFICIENCY DISEASE

PUBN-DATE: November 10, 1989

## INVENTOR-INFORMATION:

NAME	COUNTRY
KONDO, MASAHIRO	
INOUE, KUNIYO	

US-CL-CURRENT: 435/7.4; 435/960  
INT-CL. (IPC): G01N 33/573; G01N 33/577; C12N 15/00; C12P 21/00

## ABSTRACT:

PURPOSE: To specifically judge the loss of Cu and Zn-SOD (superoxide dismutase) of ischemia renal insufficiency by using a monoclonal antibody specific to Cu and Zn-SOD to be detected.

CONSTITUTION: The kidney structure is dyed by using a reagent for immune tissue dyeing formed by labeling the monoclonal antibody to be conjugated specifically with the Cu and Zn-SOD with a labeling material to detect the Cu and Zn-SOD. The monoclonal antibody to be used is obtd. by conjugating the antibody producing spleen cells of an animal immunized by the Cu and Zn-SOD and myeloma cells thereof to obtain the hybridoma producing the monoclonal antibody for labeling the Cu and Zn-SOD, then culturing the hybridoma and/or the cell strains derived therefrom and taking the monoclonal antibody from the cultured matter thereof. The dyed tissue sample can be observed by an optical microscope if the labeling material is enzyme and by a fluorescent microscope if said material is a fluorescent material.

COPYRIGHT: (C) 1989, JPO&amp;Japio

L9: Entry 1 of 3

File: JPAB

Nov 10, 1989

DOCUMENT-IDENTIFIER: JP 01280255 A  
TITLE: INSPECTION OF RENAL INSUFFICIENCY DISEASE

## FPAR:

PURPOSE: To specifically judge the loss of Cu and Zn-SOD (superoxide dismutase) of ischemia renal insufficiency by using a monoclonal antibody specific to Cu and Zn-SOD to be detected.

## FPAR:

CONSTITUTION: The kidney structure is dyed by using a reagent for immune tissue dyeing formed by labeling the monoclonal antibody to be conjugated specifically with the Cu and Zn-SOD with a labeling material to detect the Cu and Zn-SOD. The monoclonal antibody to be used is obtd. by conjugating the antibody producing spleen cells of an animal immunized by the Cu and Zn-SOD and myeloma cells thereof to obtain the hybridoma producing the monoclonal antibody for labeling the Cu and Zn-SOD, then culturing the hybridoma and/or the cell strains derived therefrom and taking the monoclonal antibody from the cultured matter thereof. The dyed tissue sample can be observed by an optical microscope if the labeling material is enzyme and by a fluorescent microscope if said material is a fluorescent material.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KWC](#) | [Draw Desc](#) | [Image](#)

---

2. Document ID: JP 01165963 A

L9: Entry 2 of 3

File: JPAB

Jun 29, 1989

PUB-NO: JP401165963A

DOCUMENT-IDENTIFIER: JP 01165963 A

TITLE: MEASURING METHOD OF CU, ZN-SUPEROXIDE DISMUTASE

PUBN-DATE: June 29, 1989

INVENTOR-INFORMATION:

NAME COUNTRY

AITSU, SHUNICHI

KONDO, MASAHIKE

INOUE, KUNIYO

INT-CL (IPC): G01N 33/573; C12Q 1/00; C12Q 1/26; G01N 33/577

ABSTRACT:

PURPOSE: To simplify an operation by a method wherein a monoclonal antibody recognizing Cu, Zn-superoxide dismutase (SOD) is used, an antibody made to be solid-phase and an antibody made to be marked are the same antibody, antigen-antibody reactions are conducted in the same vessel, and the sensitivity in measurement is set to be 1&sim;320ng/ml.

CONSTITUTION: A monoclonal antibody recognizing Cu, Zn-SOD peculiarly is used, an antibody made to be solid-phase and a recognized antibody are the same antibodies, antigen-antibody reactions are conducted simultaneously in the same vessel by using these antibodies, and the sensitivity in measurement is set to be 1&sim;320ng/ml. The monoclonal antibody is obtained in the following means. Hybridoma producing the monoclonal antibody recognizing Cu, Zn-SOD is obtained by fusing an antibody-producing splenic cell of an animal immunized by Cu, Zn-SOD and a myeloma cell preferably, then the hybridoma and/or a cell stock derived therefrom are cultured, and the monoclonal antibody is collected from the

culture. Said hybridoma can be prepared by a cell fusion method.

COPYRIGHT: (C)1989,JPO&Japio

L9: Entry 2 of 3

File: JPAB

Jun 29, 1989

DOCUMENT-IDENTIFIER: JP 01165963 A

TITLE: MEASURING METHOD OF CU, ZN-SUPEROXIDE DISMUTASE

FFPAR:

PURPOSE: To simplify an operation by a method wherein a monoclonal antibody recognizing Cu, Zn-superoxide dismutase (SOD) is used, an antibody made to be solid-phase and an antibody made to be marked are the same antibody, antigen-antibody reactions are conducted in the same vessel, and the sensitivity in measurement is set to be 1<sim>320ng/ml.

FFPAR:

CONSTITUTION: A monoclonal antibody recognizing Cu, Zn-SOD peculiarly is used, an antibody made to be solid-phase and a recognized antibody are the same antibodies, antigen-antibody reactions are conducted simultaneously in the same vessel by using these antibodies, and the sensitivity in measurement is set to be 1<sim>320ng/ml. The monoclonal antibody is obtained in the following means. Hybridoma producing the monoclonal antibody recognizing Cu, Zn-SOD is obtained by fusing an antibody-producing splenic cell of an animal immunized by Cu, Zn-SOD and a myeloma cell preferably, then the hybridoma and/or a cell stock derived therefrom are cultured, and the monoclonal antibody is collected from the culture. Said hybridoma can be prepared by a cell fusion method.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KOMC](#) | [Drawn Desc](#) | [Image](#)

---

3. Document ID: JP 63301800 A

L9: Entry 3 of 3

File: DWPI

Dec 8, 1988

DERWENT-ACC-NO: 1989-028190

DERWENT-WEEK: 198904

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Measuring copper and zinc superoxidizedismutase - by sandwich method using two monoclonal antibodies which recognise both cpds. and marking

PRIORITY-DATA: 1987JP-0133507 (May 30, 1987)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 63301800 A	December 8, 1988		004	

INT-CL (IPC): C12Q 1/26

ABSTRACTED-PUB-NO: JP63301800A

BASIC-ABSTRACT:

The method is characterised by measuring Cu, Zn-superoxide dismutase (Cu, zn-SOD) by the sandwich method using two kinds of monoclonal antibodies which recognise Cu, Zn-SOD, that is, (A) fixed antibody 1 and (B) antibody 2 which recognises the different part of the antigen in Cu, Zn-SOD and is marked with the marker.

The monoclonal antibodies are prep'd. by (a) fusing antibody-producing spleen cells of the animal immunised with Cu, Zn-SOD and myeloma cells for obtaining the hybridoma which produces the monoclonal antibody recognising the Cu, Zn-SOD, (b) culturing the hybridoma and/or the cell strain originated from the hybridoma and (c) collecting the monoclonal antibody from the culture prod.

USE/ADVANTAGE - The measurement can be effected correctly, even the substance which can eliminate superoxide other than Cu, Zn-SOD. The monoclonal antibodies can be obtd. in large quantities with homogeneous quality and the homogeneous reaction can be obtd.

L9: Entry 3 of 3

File: DWPI

Dec 8, 1988

DERWENT-ACC-NO: 1989-028190

DERWENT-WEEK: 198904

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Measuring copper and zinc superoxidizedismutase - by sandwich method using two monoclonal antibodies which recognise both cpds. and marking

ABTX:

The method is characterised by measuring Cu, Zn-superoxide dismutase (Cu, zn-SOD) by the sandwich method using two kinds of monoclonal antibodies which recognise Cu, Zn-SOD, that is, (A) fixed antibody 1 and (B) antibody 2 which recognises the different part of the antigen in Cu, Zn-SOD and is marked with the marker.

ABTX:

The monoclonal antibodies are prep'd. by (a) fusing antibody-producing spleen cells of the animal immunised with Cu, Zn-SOD and myeloma cells for obtaining the hybridoma which produces the monoclonal antibody recognising the Cu, Zn-SOD, (b) culturing the hybridoma and/or the cell strain originated from the hybridoma and (c) collecting the monoclonal antibody from the culture prod.

ABTX:

USE/ADVANTAGE - The measurement can be effected correctly, even the substance which can eliminate superoxide other than Cu, Zn-SOD. The monoclonal antibodies can be obtd. in large quantities with homogeneous quality and the homogeneous reaction can be obtd.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)[KMC](#) | [Draw Desc](#) | [Image](#)[Generate Collection](#)

Term	Documents
(7 NOT 8).JPAB,EPAB,DWPI.	3

[Display](#)

25

Documents, starting with Document:

3

[Display Format:](#) [REV , K](#) [Change Format](#)

**WEST****Generate Collection****Search Results - Record(s) 1 through 21 of 21 returned.** **1. Document ID: JP 63301800 A**

L21: Entry 1 of 21

File: JPAB

Dec 8, 1988

PUB-N0: JP363301800A

DOCUMENT-IDENTIFIER: JP 63301800 A

TITLE: DETERMINATION OF CU,ZN-SUPEROXIDE-DISMUTASE

PUBN-DATE: December 8, 1988

## INVENTOR-INFORMATION:

NAME

COUNTRY

KONDO, MASAHIKE

INOUE, KUNIYO

US-CL-CURRENT: 435/25

INT-CL (IPC): C12Q 1/26

## ABSTRACT:

PURPOSE: To easily determine Cu,Zn-superoxide.dismutase (Cu,Zn-SOD) useful in the field of immunology, etc., in high uniformity of reaction, by using a specific monoclonal antibody.

CONSTITUTION: An antibody-producing spleen cell of an animal immunized with Cu-Zn-SOD is fused with a myeloma cell to obtain a hybridoma and/or a cell strain originated from the hybridoma. The cell strain is cultured to produce a monoclonal antibody and obtain (A) the immobilized 1st antibody and (B) the 2nd antibody capable of recognizing an antigen site different from the antibody A and recognizing a Cu,Zn-SOD labeled with a labeling agent. A specimen such as serum containing human Cu,Zn-SOD is made to react with the antibodies A, B in a well and the concentration of Cu,Zn-SOD is calculated by a solid-phase enzymatic immunoassay using a sandwich process.

COPYRIGHT: (C)1988,JPO&amp;Japio

L21: Entry 1 of 21

File: JPAB

Dec 8, 1988

DOCUMENT-IDENTIFIER: JP 63301800 A  
TITLE: DETERMINATION OF Cu,ZN-SUPEROXIDE-DISMUTASE

## FPAR:

PURPOSE: To easily determine Cu,Zn-superoxide.dismutase (Cu,Zn-SOD) useful in the field of immunology, etc., in high uniformity of reaction, by using a specific monoclonal antibody.

## FPAR:

CONSTITUTION: An antibody-producing spleen cell of an animal immunized with Cu-Zn-SOD is fused with a myeloma cell to obtain a hybridoma and/or a cell strain originated from the hybridoma. The cell strain is cultured to produce a monoclonal antibody and obtain (A) the immobilized 1st antibody and (B) the 2nd antibody capable of recognizing an antigen site different from the antibody A and recognizing a Cu,Zn-SOD labeled with a labeling agent. A specimen such as serum containing human Cu,Zn-SOD is made to react with the antibodies A, B in a well and the concentration of Cu,Zn-SOD is calculated by a solid-phase enzymatic immunoassay using a sandwich process.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KJMC](#) | [Draw Desc](#) | [Image](#)

---

2. Document ID: JP 63209584 A

L21: Entry 2 of 21

File: JPAB

Aug 31, 1988

PUB-NO: JP363209584A

DOCUMENT-IDENTIFIER: JP 63209584 A

TITLE: COLLECTION OF COPPER-ZINC SUPER OXIDE DISMUTASE

PUBN-DATE: August 31, 1988

INVENTOR-INFORMATION:

NAME

COUNTRY

TOMITA, KATSUHISA

NISHIMOTO, MASAICHI

NISHIDE, MITSUYUKI

NAITO, AKINORI

KAJIWARA, JUNICHI

TAKAGI, KENKICHI

US-CL-CURRENT: 435/189; 435/849  
INT-CL (IPC): C12N 9/02; C12N 15/00

ABSTRACT:

PURPOSE: To efficiently produce activator Cu.Zn-SOD quantitatively coordinating copper zinc, by grinding culture cells of recombinant bacterium capable of producing SOC grown in a nutritive medium in a buffer solution containing a water-soluble copper salt and a water-soluble zinc salt.

CONSTITUTION: A bacterium such as Escherichia coli strain w3110 ATCC27325, etc., capable of producing SOD (superoxide dismutase), is subjected to shaking culture in L-medium consisting of casein hydrolyzate, yeast essence inorganic salt and carbon source assimilating Escherichia, coli, etc, at 30°C. When absorbance at 500nm becomes 0.2, the temperature is raised to 37°C and shaking culture is carried out further for 24hr. About 102~2030 cells, preferably 1010~1020 cells are suspended in 1l buffer solution containing Cu ion and Zn ion, ground by

ultrasonic treatment, etc., and the aimed enzyme is isolated from the supernatant liquid.

COPYRIGHT: (C)1988,JPO&Japio

L21: Entry 2 of 21

File: JPAB

Aug 31, 1988

DOCUMENT-IDENTIFIER: JP 63209584 A

TITLE: COLLECTION OF COPPER-ZINC SUPER OXIDE DISMUTASE

FPAR:

PURPOSE: To efficiently produce activator Cu.Zn-SOD quantitatively coordinating copper zinc, by grinding culture cells of recombinant bacterium capable of producing SOC grown in a nutritive medium in a buffer solution containing a water-soluble copper salt and a water-soluble zinc salt.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KJC](#) | [Draw Desc](#) | [Image](#)

---

3. Document ID: JP 63077822 A

L21: Entry 3 of 21

File: JPAB

Apr 8, 1988

PUB-NO: JP363077822A

DOCUMENT-IDENTIFIER: JP 63077822 A

TITLE: ORGAN FUNCTION IMPROVER

PUBN-DATE: April 8, 1988

INVENTOR-INFORMATION:

NAME

COUNTRY

OTSU, NORIO

AKIYAMA, NOBUO

MITA, ISASHI

TOMIKAWA, SHINJI

OTSUBO, OSAMU

FUJIWARA, HIROSHI

NAKAKOSHI, ICHIRO

US-CL-CURRENT: 435/189; 435/849

INT-CL (IPC): A61K 37/02; A61K 37/02; A61K 37/02; C12N 9/02; C12N 15/00; C12P 21/00

ABSTRACT:

PURPOSE: To obtain an organ function improver comprising a polypeptide having substantially the same amino acid sequence as that of human superoxide dismutase (SOD) as an active ingredient.

CONSTITUTION: DNA is separated from normal human tissue (e.g. liver, placenta), mRNA (mixture containing mRNA of human Cu,Zn-SOD) having poly(A)tail is separated by the use of oligo(dT)cellulose and poly(U)Sepharose and cDNA of human Cu,Zn-SOD is synthesized by using the mRNA. A self-replicative vector is integrated with a DNA fragment (preferably fragment of colicin E1 gene having positive regulation site) containing character manifestation regulating gene and a structural gene fragment of human Cu,Zn-SOD to give the aimed recombinant DNA. A bacterium transformed with the recombinant DNA is cultivated and human Cu,Zn-SOD accumulated in the culture mixture is collected.

COPYRIGHT: (C)1988,JPO&Japio

COPYRIGHT. (C) 1988, JPO&amp;Japio

L21: Entry 3 of 21

File: JPAB

Apr 8, 1988

DOCUMENT-IDENTIFIER: JP 63077822 A

TITLE: ORGAN FUNCTION IMPROVER

## FPAR:

CONSTITUTION: DNA is separated from normal human tissue (e.g. liver, placenta), mRNA (mixture containing mRNA of human Cu,Zn-SOD) having poly(A)tail is separated by the use of oligo(dT)cellulose and poly(U)Sephadex and cDNA of human Cu,Zn-SOD is synthesized by using the mRNA. A self-replicative vector is integrated with a DNA fragment (preferably fragment of colicin E1 gene having positive regulation site) containing character manifestation regulating gene and a structural gene fragment of human Cu,Zn-SOD to give the aimed recombinant DNA. A bacterium transformed with the recombinant DNA is cultivated and human Cu,Zn-SOD accumulated in the culture mixture is collected.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Reviews](#) | [Classification](#) | [Date](#) | [Reference](#)[KIMC](#) | [Draw Desc](#) | [Image](#) 4. Document ID: JP 62226928 A

L21: Entry 4 of 21

File: JPAB

Oct 5, 1987

PUB-NO: JP362226928A

DOCUMENT-IDENTIFIER: JP 62226928 A

TITLE: ORGAN FUNCTION IMPROVER

PUBN-DATE: October 5, 1987

## INVENTOR-INFORMATION:

NAME

COUNTRY

OTSU, NORIO

NAKAKOSHI, ICHIRO

INT-CL (IPC): A61K 37/50; A61K 35/74; A61K 37/02

## ABSTRACT:

PURPOSE: A drug for improving organ function in organ transplantation, comprising a polypeptide having substantially the same amino acid sequence as that of human superoxide dismutase as an active ingredient.

CONSTITUTION: An organ function improver comprising a polypeptide having substantially the same amino acid sequence as that of human superoxide dismutase as an active ingredient. The polypeptide, for example, can be obtained by cultivating a bacterium which is transformed with recombinant DNA containing a human copper, zinc type superoxide dismutase at the downstream of a phenotypic expression control gene having a positive regulation site and by collecting a human copper, zinc type super oxide dismutase accumulated in a culture mixture. The polypeptide is used for preserving an organ extracted from an organism as it is in a living state or injected into an organism to improve organ functions and can be prepared into injection, tablet, ointment, capsule, liposome preparation, etc.

COPYRIGHT: (C)1987,JPO&amp;Japio

L21: Entry 4 of 21

File: JPAB

Oct 5, 1987

DOCUMENT-IDENTIFIER: JP 62226928 A  
TITLE: ORGAN FUNCTION IMPROVER

## FPAR:

CONSTITUTION: An organ function improver comprising a polypeptide having substantially the same amino acid sequence as that of human superoxide dismutase as an active ingredient. The polypeptide, for example, can be obtained by cultivating a bacterium which is transformed with recombinant DNA containing a human copper, zinc type superoxide dismutase at the downstream of a phenotypic expression control gene having a positive regulation site and by collecting a human copper, zinc type super oxide dismutase accumulated in a culture mixture. The polypeptide is used for preserving an organ extracted from an organism as it is in a living state or injected into an organism to improve organ functions and can be prepared into injection, tablet, ointment, capsule, liposome preparation, etc.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KJWC](#) | [Draw Desc](#) | [Image](#)

---

5. Document ID: JP 62167479 A

L21: Entry 5 of 21

File: JPAB

Jul 23, 1987

PUB-N0: JP362167479A

DOCUMENT-IDENTIFIER: JP 62167479 A

TITLE: REAGENT FOR MEASURING HUMAN COPPER/ZINC-SUPEROXIDE DISMUTASE COMPRISING MONOCLONAL ANTIBODY OF HUMAN COPPER/ZINC SUPEROXIDE DISMUTASE AND DIAGNOSIS OF STOMACH CANCER USING SAME

PUBN-DATE: July 23, 1987

INVENTOR-INFORMATION:

NAME

COUNTRY

UDA, TAIZO

NOJI, SHIRO

USAGAWA, TAKASHI

UMEDA, KAZUHIRO

INT-CL (IPC): G01N 33/573; C12P 21/00; G01N 33/577; C07K 15/04; C12N 9/02

ABSTRACT:

PURPOSE: To easily perform the diagnosis of stomach cancer, by measuring the concn. of human copper/zinc-superoxide dimutase (Cu.Zn-SOD) using a diagnostic/examination agent comprising a monocronal antibody specific to Cu.Z-SOD.

CONSTITUTION: In preparing a monoclonal antibody, SOD (purity; 95% or more) occurring from a human erythrocyte is allowed to immunize, for example, a BALB/c mouse and, after the spleen is extracted, mouse myeloma cells of SP2 or NS-1 are fused using ethylene glycol and hybridoma is obtained according to a usual method. A predetermined amount of the hybridoma is transplanted to the abdominal cavity of a mouse to which pristan (2, 6, 10, 14-tetramethylpentadecane) was preliminarily administered and after 1&sim;2 weeks, abdominal dopsy is collected and purified using ion exchange chromatography to obtain a large amount of the monoclonal antibody. A diagnostic/examination agent comprising the monoclonal antibody specific to Cu.Zn-SOD is used and the concn. of Cu-Zn-SOD is measured to make it possible to easily diagnose stomach center.

COPYRIGHT: (C) 1987, JPO&Japio

L21: Entry 5 of 21

File: JPAB

Jul 23, 1987

DOCUMENT-IDENTIFIER: JP 62167479 A

TITLE: REAGENT FOR MEASURING HUMAN COPPER/ZINC-SUPEROXIDE DISMUTASE COMPRISING MONOCLONAL ANTIBODY OF HUMAN COPPER/ZINC SUPEROXIDE DISMUTASE AND DIAGNOSIS OF STOMACH CANCER USING SAME

FPAR:

CONSTITUTION: In preparing a monoclonal antibody, SOD (purity; 95% or more) occur ring from a human erythrocyte is allowed to immunize, for example, a BALB/c mouse and, after the spleen is extracted, mouse myeloma cells of SP2 or NS-1 are fused using ethylene glycol and hybridoma is obtained according to a usual method. A predetermined amount of the hybridoma is transplanted to the abdominal cavity of a mouse to which pristan (2, 6, 10, 14-tetramethylpentadecane) was preliminarily administered and after 1&sim;2 weeks, abdominal dopsy is collected and purified using ion exchange chromatography to obtain a large amount of the monoclonal antibody. A diagnostic/examination agent comprising the monoclonal antibody specific to Cu.Zn-SOD is used and the concn. of Cu-Zn-SOD is measured to make it possible to easily diagnose stomach center.

[ Full | Title | Citation | Front | Review | Classification | Date | Reference ]

[ KMC | Draw Desc | Image ]

---

6. Document ID: JP 61212600 A

L21: Entry 6 of 21

File: JPAB

Sep 20, 1986

PUB-NO: JP361212600A

DOCUMENT-IDENTIFIER: JP 61212600 A

TITLE: MONOCLONAL ANTIBODY TO HUMAN COPPER, ZINC SUPEROXIDE DISMUTASE AND PRODUCTION THEREOF

PUBN-DATE: September 20, 1986

INVENTOR-INFORMATION:

NAME

COUNTRY

UDA, TAIZO

KUMAHARA, HIROMI

NOJI, SHIRO

USAGAWA, TAKASHI

US-CL-CURRENT: 435/FOR.111; 435/FOR.125, 435/6, 435/332, 530/388.26

INT-CL (IPC): C07K 15/04; A61K 39/395; C12N 15/00; C12P 21/00; G01N 33/573; G01N 33/577

ABSTRACT:

PURPOSE: To obtain the titled antibody suitable for the determination of human copper, zinc superoxide dismutase (Cu, Zn-SOD), by immunizing an animal with Cu, Zn-SOD, and using the hybridoma of the lymphocyte of said animal and a myeloma cell.

CONSTITUTION: Lymphocyte prepared from the lymph node or spleen of an animal (e.g. mouse, rat, etc.) immunized with human Cu, Zn-SOD is subjected to the cell fusion with a myeloma cell (e.g. P3U1, NS-1, etc., originated from mouse), and the obtained hybridoma is cloned to obtain a clone capable of producing an anti-human Cu, Nz-SOD monoclonal antibody. The objective antibody can be produced by the tissue culture of the clone or the culture of the clone in the abdominal cavity of a small animal.

COPYRIGHT: (C)1986,JPO&Japio

L21: Entry 6 of 21

File: JPAB

Sep 20, 1986

DOCUMENT-IDENTIFIER: JP 61212600 A

TITLE: MONOCLONAL ANTIBODY TO HUMAN COPPER, ZINC SUPEROXIDE DISMUTASE AND PRODUCTION THEREOF

FPAR:

PURPOSE: To obtain the titled antibody suitable for the determination of human copper, zinc superoxide dismutase (Cu, Zn-SOD), by immunizing an animal with Cu, Zn-SOD, and using the hybridoma of the lymphocyte of said animal and a myeloma cell.

FPAR:

CONSTITUTION: Lymphocyte prepared from the lymph node or spleen of an animal (e.g. mouse, rat, etc.) immunized with human Cu, Zn-SOD is subjected to the cell fusion with a myeloma cell (e.g. P3U1, NS-1, etc., originated from mouse), and the obtained hybridoma is cloned to obtain a clone capable of producing an anti-human Cu, Nz-SOD monoclonal antibody. The objective antibody can be produced by the tissue culture of the clone or the culture of the clone in the abdominal cavity of a small animal.

7. Document ID: US 5360729 A

L21: Entry 7 of 21

File: EPAB

Nov 1, 1994

PUB-N0: US005360729A

DOCUMENT-IDENTIFIER: US 5360729 A

TITLE: Method for purification of recombinant copper/zinc (CU-ZN) superoxide dismutase from bacteria or eucaryotic cells

PUBN-DATE: November 1, 1994

## INVENTOR-INFORMATION:

NAME	COUNTRY
BARTFELD, DANIEL	CA
LIESHITZ, RUTH	IL
HADARY, DANY	CA

INT-CL (IPC): C12N 9/02

EUR-CL (EPC): C12N009/02

## ABSTRACT:

The subject invention provides a method for recovering a solution containing purified, enzymatically active Cu-Zn superoxide dismutase or a polypeptide analog thereof having substantially the same amino acid sequence as, and the biological activity of, naturally-occurring Cu-Zn superoxide dismutase from a composition which comprises cells containing Cu-Zn superoxide dismutase or a polypeptide analog thereof. The invention also provides a method of increasing the yield of recovered solutions having an increased concentration of b isoform of an enzymatically-active polypeptide analog of Cu-Zn superoxide dismutase from a composition which comprises cells containing a, b and c isoforms of the polypeptide analog.

L21: Entry 7 of 21

File: EPAB

Nov 1, 1994

DOCUMENT-IDENTIFIER: US 5360729 A

TITLE: Method for purification of recombinant copper/zinc (CU-ZN) superoxide dismutase from bacteria or eucaryotic cells[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)[Image](#) | [Draw Desc](#) | [Image](#) 8. Document ID: US 5112744 A

L21: Entry 8 of 21

File: EPAB

May 12, 1992

PUB-NO: US005112744A

DOCUMENT-IDENTIFIER: US 5112744 A

TITLE: Plasmids for the production of human Cu-Zn superoxide dismutase, bacterial hosts containing the plasmids and methods for production and recovery of such superoxide dismutase

PUBN-DATE: May 12, 1992

INVENTOR-INFORMATION:

NAME	COUNTRY
OPPENHEIM, AMOS B	IL
LEVANON, AVIGDOR	IL
LOCKER-GALADI, HILLA	IL
GORECKI, MARIAN	IL

INT-CL (IPC): C12N 1/21; C12N 9/02; C12N 15/00; C12N 15/73

EUR-CL (EPC): C07K014/61; C07K014/775, C12N009/02 , C12N015/73 , A23K001/165 , A61K038/44 , C12N015/69

ABSTRACT:

An improved vector upon introduction into a suitable host containing the thermolabile repressor CI renders the host capable of effecting expression of a desired gene. The vector is a double-stranded DNA molecule which includes in 5' to 3' order the following: the promoter and operator PLOL from lambda bacteriophage; the N utilization site; a first restriction enzyme site permitting replacement of the ribosomal binding site which follows thereafter; a ribosomal binding site; and ATG initiation codon or DNA which is converted into and ATG initiation codon upon insertion of the desired gene into the vector; a second restriction enzyme site for inserting the gene in phase with the ATG codon; a T1T2 rRNA transcription termination sequence; and origin of replication and a gene associated with a selectable or identifiable phenotypic trait manifested when the vector is present in the host. The distance between the 3' end of the PLOL promotor and operator sequence and the 5' end of the N utilization site is less than about 80 base pairs and the distance between the 3' end of the N utilization site and the 5' end of the ribosomal binding site is less than about 300 base pairs. Plasmids have been constructed from the vectors and used to produce bovine, chicken and porcine growth hormones, human apolipoprotein E and human superoxide dismutase.

L21: Entry 8 of 21

File: EPAB

May 12, 1992

DOCUMENT-IDENTIFIER: US 5112744 A

TITLE: Plasmids for the production of human Cu-Zn superoxide dismutase, bacterial hosts containing the plasmids and methods for production and recovery of such superoxide dismutase

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KuMC](#) | [Drawn Desc](#) | [Image](#)

9. Document ID: US 5066591 A

L21: Entry 9 of 21

File: EPAB

Nov 19, 1991

PUB-NO: US005066591A

DOCUMENT-IDENTIFIER: US 5066591 A

TITLE: Polypeptides of human copper/zinc superoxide dimutase

PUBN-DATE: November 19, 1991

INVENTOR-INFORMATION:

NAME

COUNTRY

HALLEWELL, ROBERT A

US

MULLENBACH, GUY T

US

INT-CL (IPC): C12N 9/02; C12N 15/03

EUR-CL (EPC): C12N009/02; C12N015/62, C12N015/70 , C12N015/81

ABSTRACT:

Methods and compositions are provided for the production of human copper/zinc superoxide dimutase (SOD) polypeptides in microorganisms. Bacterially produced human CuZn SOD polypeptides are provided. E. coli strain D1210 (pSODX8) was deposited at the A.T.C.C. on Sept. 27, 1983 and given Accession No. 39453. Yeast strain 2150-2-3 (pCl/1GAPSOD) and E. coli strains D1210 (pSOD11) and D1210 (pS2OR) were deposited at the A.T.C.C. on May 9, 1984, and were given Accession Nos. 20708, 39679 and 39680, respectively.

L21: Entry 9 of 21

File: EPAB

Nov 19, 1991

DOCUMENT-IDENTIFIER: US 5066591 A

TITLE: Polypeptides of human copper/zinc superoxide dimutase

FPAR:

Methods and compositions are provided for the production of human copper/zinc superoxide dimutase (SOD) polypeptides in microorganisms. Bacterially produced human CuZn SOD polypeptides are provided. E. coli strain D1210 (pSODX8) was deposited at the A.T.C.C. on Sept. 27, 1983 and given Accession No. 39453. Yeast strain 2150-2-3 (pCl/1GAPSOD) and E. coli strains D1210 (pSOD11) and D1210 (pS2OR) were deposited at the A.T.C.C. on May 9, 1984, and were given Accession Nos. 20708, 39679 and 39680, respectively.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMC](#) | [Drawn Desc](#) | [Image](#)

---

10. Document ID: WO 9106634 A1

L21: Entry 10 of 21

File: EPAB

May 16, 1991

PUB-NO: WO009106634A1

DOCUMENT-IDENTIFIER: WO 9106634 A1

TITLE: IMPROVED METHOD FOR PURIFICATION OF RECOMBINANT COPPER/ZINC (CU-ZN)  
SUPEROXIDE DISMUTASE FROM BACTERIA OR EUKARYOTIC CELLS

PUBN-DATE: May 16, 1991

INVENTOR-INFORMATION:

NAME	COUNTRY
BARTFELD, DANIEL	CA
LIFSHITZ, RUTH	IL
HADARY, DANY	CA

US-CL-CURRENT: 435/189

INT-CL (IPC): C12N 9/02

EUR-CL (EPC): C12N009/02

ABSTRACT:

The subject invention provides a method for recovering a solution containing purified, enzymatically active Cu-Zn superoxide dismutase or a polypeptide analog thereof having substantially the same amino acid sequence as, and the biological activity of, naturally-occurring Cu-Zn superoxide dismutase from a composition which comprises cells containing Cu-Zn superoxide dismutase or a polypeptide analog thereof. The invention also provides a method of increasing the yield of recovered solutions having an increased concentration of b isoform of an enzymatically-active polypeptide analog of Cu-Zn superoxide dismutase from a composition which comprises cells containing a, b and c isoforms of the polypeptide analog.

L21: Entry 10 of 21

File: EPAB

May 16, 1991

DOCUMENT-IDENTIFIER: WO 9106634 A1

TITLE: IMPROVED METHOD FOR PURIFICATION OF RECOMBINANT COPPER/ZINC (CU-ZN)  
SUPEROXIDE DISMUTASE FROM BACTERIA OR EUKARYOTIC CELLS

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) |

[Kwic](#) | [Drawn Desc](#) | [Clip Img](#) | [Image](#) |

---

11. Document ID: US 4029819 A

L21: Entry 11 of 21

File: EPAB

Jun 14, 1977

PUB-NO: US004029819A

DOCUMENT-IDENTIFIER: US 4029819 A

TITLE: Superoxide dismutase and its application as an oxidation inhibitor

PUBN-DATE: June 14, 1977

INVENTOR-INFORMATION:

NAME

COUNTRY

MICHELSON, ADOLF MICHAEL

INT-CL (IPC): A23L 3/34

EUR-CL (EPC): C12N009/02; A23L003/3463

ABSTRACT:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 +/- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

L21: Entry 11 of 21

File: EPAB

Jun 14, 1977

DOCUMENT-IDENTIFIER: US 4029819 A

TITLE: Superoxide dismutase and its application as an oxidation inhibitor

FPAR:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 +/- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

[Full](#) [Title](#) [Citation](#) [Front](#) [Review](#) [Classification](#) [Date](#) [Reference](#)

[KDDC](#) [Drawn Desc](#) [Image](#)

---

12. Document ID: US 3997402 A

L21: Entry 12 of 21

File: EPAB

Dec 14, 1976

PUB-N0: US003997402A  
DOCUMENT-IDENTIFIER: US 3997402 A  
TITLE: Superoxide dismutase and process for production

PUBN-DATE: December 14, 1976

INVENTOR-INFORMATION:

NAME	COUNTRY
MICHELSON, ADOLF MICHAEL	

INT-CL (IPC): C07G 7/026  
EUR-CL (EPC): A23L003/3463; C12N009/02

ABSTRACT:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 +/- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

L21: Entry 12 of 21

File: EPAB

Dec 14, 1976

DOCUMENT-IDENTIFIER: US 3997402 A  
TITLE: Superoxide dismutase and process for production

FPAR:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 +/- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) |

[RDMC](#) | [Drawn Desc](#) | [Image](#)

---

13. Document ID: US 5162217 A

L21: Entry 13 of 21

File: DWPI

Nov 10, 1992

DERWENT-ACC-NO: 1992-398025

DERWENT-WEEK: 200018

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Plasmid for prodn. of super:oxide dismutase - using Escherichia coli host cell contg. temp. sensitive repressor

INVENTOR: AVIV, H; GORECKI, M ; HARTMAN, J R ; OPPENHEIM, A B ; OREN, R

PRIORITY-DATA: 1986US-0897056 (August 14, 1986), 1984US-0644245 (August 27, 1984), 1985US-0767143 (August 19, 1985), 1988US-0202238 (June 3, 1988), 1989US-0449125 (December 8, 1989)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5162217 A	November 10, 1992		061	C12N009/02

INT-CL (IPC): C12N 9/02; C12N 15/70

ABSTRACTED-PUB-NO: US 5162217A

BASIC-ABSTRACT:

Plasmid comprises: (a) a double-stranded (ds) DNA molecule including, 3'-5', (i) an N-utilisation site selected from NutL and NutR, for blinding anti-terminator N protein, produced by an E.coli host cell; and (ii) a DNA sequence contg. the bacteriophage promoter/operator (PLOL); (b) a DNA sequence contg. the naturally-occurring beta lactamase RBS from pBR322; (c) an initiation cochoin, ATG; (d) DNA encoding the Cu-Zn SOD polypeptide analogue; and (e) DNA contg. an origin of replication (ORI) from pBR322 capable of autonomous replication in E.coli and a sequence contg. a gene associated with a selectable or identifiable phenotypic trait, manifested when the plasmid is present in the E.coli cell. Also claimed are: pref. when the plasmid is introduced into a suitable E.coli host cell contg. the thermolabile repressor, CI, the cell is rendered capable, upon increasing the host cell temperature to inactivate the repressor, of effecting expression of DNA encoding the Cu-Zn SOD analogue.

USE - Plasmid is useful, in a host-vector system, for producing human SOD and analogues which may in turn be used to catalyse the reduction of superoxide radicals, reduce reperfusion injury, prolong the survival time of isolated organs and reduce spinal cord injury

L21: Entry 13 of 21

File: DWPI

Nov 10, 1992

DERWENT-ACC-NO: 1992-398025  
DERWENT-WEEK: 200018  
COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Plasmid for prodn. of super:oxide dismutase - using Escherichia coli host cell contg. temp. sensitive repressor

ABTX:

Plasmid comprises: (a) a double-stranded (ds) DNA molecule including, 3'-5', (i) an N-utilisation site selected from NutL and NutR, for blinding anti-terminator N protein, produced by an E.coli host cell; and (ii) a DNA sequence contg. the bacteriophage promoter/operator (PLOL); (b) a DNA sequence contg. the naturally-occurring beta lactamase RBS from pBR322; (c) an initiation cochoin, ATG; (d) DNA encoding the Cu-Zn SOD polypeptide analogue; and (e) DNA contg. an origin of replication (ORI) from pBR322 capable of autonomous replication in E.coli and a sequence contg. a gene associated with a selectable or identifiable phenotypic trait, manifested when the plasmid is present in the E.coli cell. Also claimed are: pref. when the plasmid is introduced into a suitable E.coli host cell contg. the thermolabile repressor, CI, the cell is rendered capable, upon increasing the host cell temperature to inactivate the repressor, of effecting expression of DNA encoding the Cu-Zn SOD analogue.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMC](#) | [Draw](#) [Desc](#) | [Image](#)

---

14. Document ID: US 5143836 A

L21: Entry 14 of 21

File: DWPI

Sep 1, 1992

DERWENT-ACC-NO: 1992-315517  
DERWENT-WEEK: 199833  
COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Plasmids for prodn. of human super-oxide dismutase analogues - contain lambda promoter and operator, N utilisation site and ribosomal binding site, used for treating inflammation and preventing onco-genesis

INVENTOR: AVIV, H; GORECKI, M ; HARTMAN, J R ; OPPENHEIM, A B

PRIORITY-DATA: 1985US-0767143 (August 19, 1985), 1984US-0644245 (August 27, 1984), 1988US-0194424 (May 13, 1988)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 5143836 A	September 1, 1992		046	C12N009/02

INT-CL (IPC): C12N 9/02; C12N 15/70

ABSTRACTED-PUB-NO: US 5143836A

BASIC-ABSTRACT:

A plasmid is claimed for the prodn. of an enzymatically active polypeptide analogue of human Cu-Zn superoxide dismutase (SOD) having the identical aminoacid sequence as, and the biological activity of, naturally-occurring human Cu-Zn SOD but an N-terminus which is not acetylated which upon introduction into a suitable E. coli host cell contg. the thermolabile repressor CI renders the host cell capable, upon increasing the temp. of the host cell to a temp. at which the repressor is inactivated, of effecting expression of DNA encoding the human Cu-Zn SOD polypeptide analogue. The plasmid comprises a double-stranded DNA molecule which comprises in 5' to 3' order: (a) a DNA sequence which contains the promoter

and operator PL OL from lambda bacteriophage. (b) an N utilisation site selected from NutL and NutR for binding anti-terminator protein produced by E. coli host cells, (c) a first unique restriction enzyme site which is EcoRI, (d) a DNA sequence which contains a ribosomal binding site selected from the natural beta-lactamase ribosomal binding site derived from pBR233 and the synthetic ribosomal binding site having the sequence AATTCAATAATATT GAAAAAGGAAGAG GTTATTATAAC TTTTCCTTCAT (I), (e) an ATG initiation codon, (f) a second unique restriction enzyme site which is NdeI and (g) DNA encoding the human Cu-Zn SOD polypeptide analogue inserted into the NdeI restriction enzyme site in phase with the ATG initiation codon; and which additionally includes a DNA sequence which contains an origin of replication from a bacterial plasmid pBR322 capable of autonomous replication in the E. coli host cell and a DNA sequence which contains a gene associated with a selectable or identifiable phenotype trait (e.g. drug resistance to ampicillin or tetracycline) which is manifested when the plasmid is present in the E. coli host cell, the distance between the 3' end of the PL OL promoter and operator sequence and the 5' end of the N utilisation site being less than 80 bp and the distance between the 3' end of the N utilisation site and the 5' end of the ribosomal binding site being less than 300 bp.

USE - The SOD and analogues are useful for treating inflammation, partic. for treating inflamed tendons in hoses. They can also be used for the prevention of oncogenesis and tumour promotion and redn. of cytotoxic and cardiotoxic effects of anti-cancer drugs, protection of ischemic tissues and protection of spermatozoa. They can also be used to reduce reperfusion injury following ischemia or organ transplantation and to prolong the survival period of excised isolated organs. They can also be used for spinal cord ischemia and for bronchial pulmonary dysplasi

L21: Entry 14 of 21

File: DWPI

Sep 1, 1992

DERWENT-ACC-NO: 1992-315517

DERWENT-WEEK: 199833

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Plasmids for prodn. of human super-oxide dismutase analogues - contain lambda promoter and operator, N utilisation site and ribosomal binding site, used for treating inflammation and preventing onco-genesis

ABTX:

A plasmid is claimed for the prodn. of an enzymatically active polypeptide analogue of human Cu-Zn superoxide dismutase (SOD) having the identical aminoacid sequence as, and the biological activity of, naturally-occurring human Cu-Zn SOD but an N-terminus which is not acetylated which upon introduction into a suitable E. coli host cell contg. the thermolabil e repressor CI renders the host cell capable, upon increasing the temp. of the host cell to a temp. at which the repressor is inactivated, of effecting expression of DNA encoding the human Cu-Zn SOD polypeptide analogue. The plasmid comprises a double-stranded DNA molecule which comprises in 5' to 3' order: (a) a DNA sequence which contains the promoter and operator PL OL from lambda bacteriophage. (b) an N utilisation site selected from NutL and NutR for binding anti-terminator protein produced by E. coli host cells, (c) a first unique restriction enzyme site which is EcoRI, (d) a DNA sequence which contains a ribosomal binding site selected from the natural beta-lactamase ribosomal binding site derived from pBR233 and the synthetic ribosomal binding site having the sequence AATTCAATAATATT GAAAAAGGAAGAG GTTATTATAAC TTTTCCTTCAT (I), (e) an ATG initiation codon, (f) a second unique restriction enzyme site which is NdeI and (g) DNA encoding the human Cu-Zn SOD polypeptide analogue inserted into the NdeI restriction enzyme site in phase with the ATG initiation codon; and which additionally includes a DNA sequence which contains an origin of replication from a bacterial plasmid pBR322 capable of autonomous replication in the E. coli host cell and a DNA sequence which contains a gene associated with a selectable or identifiable phenotype trait (e.g. drug resistance to ampicillin or tetracycline) which is manifested when the plasmid is present in the E. coil host cell, the distance between the 3' end of the PL OL promoter and operator sequence and the 5' end of the N utilisation site being less than 80 bp and the distance between the 3' end of the N utilisation site and the 5' end of the ribosomal binding site being less than 300 bp

LESS LINES SEE UP.

[Full | Title | Citation | Front | Review | Classification | Date | Reference]

[KWC | Draw Desc | Image]

---

15. Document ID: DE 3588216 G, EP 483113 A, US 5126252 A, US 5147789  
A, EP 483113 A3, EP 483113 B1

L21: Entry 15 of 21

File: DWPI

Oct 28, 1999

DERWENT-ACC-NO: 1992-143149

DERWENT-WEEK: 199951

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Human copper-zinc super oxide dismutase polypeptide analogue prodn. - by culturing transformed bacterial cells in zinc-contg. prodn. medium contg. copper ions for ischaemia treatment

INVENTOR: AVIV, H; BARTFIELD, D ; GORECKI, M ; HARTMAN, J R ; KANNER, D ; LEVANON, A ; LOCKER-GILADI, H ; OPPENHEIM, A B ; LOCKERGILA, H ; LOCKER-GALADI, H

PRIORITY-DATA: 1984US-0645119 (August 27, 1984), 1984US-0644105 (August 27, 1984), 1984US-0644245 (August 27, 1984), 1984US-0644551 (August 27, 1984), 1984US-0644671 (August 27, 1984), 1989US-0317434 (March 1, 1989), 1989US-0317629 (March 1, 1989), 1991US-0780353 (October 22, 1991)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DE 3588216 G	October 28, 1999		000	C12N015/53
EP 483113 A	April 29, 1992	E	102	
US 5126252 A	June 30, 1992		038	C12N015/18
US 5147789 A	September 15, 1992		023	C12P021/02
EP 483113 A3	May 13, 1992		000	
EP 483113 B1	September 22, 1999	E	000	C12N015/53

INT-CL (IPC): A61K 35/74; A61K 37/50; C07G 17/00; C07H 21/04; C07K 13/00; C07K 15/12; C12N 1/20; C12N 1/21; C12N 9/02; C12N 15/00; C12N 15/18; C12N 15/53; C12N 15/63; C12N 15/70; C12N 15/73; C12P 3/00; C12P 7/00; C12P 19/34; C12P 21/02; C12R 1/19

ABSTRACTED-PUB-NO: EP 483113A

BASIC-ABSTRACT:

Prodn. comprises (a) growing a culture of bacterial cells in a zinc-contg. prodn. medium supplemented with a non-growth inhibiting amt. of Cu<sup>2+</sup> so final concn. of Cu<sup>2+</sup> in the medium is more than 2 ppm, where the cells contain and express DNA encoding the polypeptide analogue of human Cu/Zn SOD and where the culture is grown under pref. conditions to express DNA and produce polypeptide in the bacterial cells and (b) recovering obtd. enzymatically active analogue of human Cu/Zn SOD etc.

USE/ADVANTAGE - Used for catalysing the redn. of superoxide radicals, reducing injury due to reperfusion following ischaemia or organ transplantation, to reduce cardiac infarct size, to increase survival time of excised isolated organs to reduce spinal cord injury, for bronchial pulmonary dysplasia, for treatment of inflammation, for prevention of oncogenesis and tumour promotion, redn. of cyto and cardio-toxic effects of anticancer drugs, for protection of ischaemic tissues, for protection of spermatozoa or for preventing neurological inj

ABSTRACTED-PUB-NO:

## EP 483113B EQUIVALENT-ABSTRACTS:

Prodn. comprises (a) growing a culture of bacterial cells in a zinc-contg. prodn. medium supplemented with a non-growth inhibiting amt. of Cu<sup>2+</sup> so final concn. of Cu<sup>2+</sup> in the medium is more than 2 ppm, where the cells contain and express DNA encoding the polypeptide analogue of human Cu/Zn SOD and where the culture is grown under pref. conditions to express DNA and produce polypeptide in the bacterial cells and (b) recovering obtd. enzymatically active analogue of human Cu/Zn SOD etc.

USE/ADVANTAGE - Used for catalysing the redn. of superoxide radicals, reducing injury due to reperfusion following ischaemia or organ transplantation, to reduce cardiac infarct size, to increase survival time of excised isolated organs to reduce spinal cord injury, for bronchial pulmonary dysplasia, for treatment of inflammation, for prevention of oncogenesis and tumour promotion, redn. of cyto and cardio-toxic effects of anticancer drugs, for protection of ischaemic tissues, for protection of spermatozoa or for preventing neurological inj

US 5126252A

Plasmid for the prodn. of bovine or porcine growth hormone or their active polypeptide fragments or analogues comprises a double stranded DNA contg. in the order 5' to 3' a promoter PLOL (from a lambda-bacteriophage); a single N-utilisation site for binding non-terminal protein NutL; a sequence TAAGGAAGTACTTACATATTCTTCATGAATGTA contg. the mutant CII ribosomal binding site (from a lambda-bacteriophage); an NdeI restriction enzyme site including an ATG initiation codon; a sequence that encodes the prodn. of the growth hormone or its active fragments; sequence contg. a T1T2 rRNA transcription termination gp.; and an origin of replication (from the bacterial plasmid pBR322).

USE - Escherichia coli cells are transformed with these plasmids and propagated to produce bovine or porcine growth hormone or corresp. active fragments or analogues.

US 5147789A

Plasmid for producing a polypeptide analogue of an animal growth hormone which has the same amino acid sequence and biological activity of a growth hormone and which, when introduced into an Escherichia coli host contg. the thermolabile repressor CI, renders the host cell capable of effecting the expression of DNA encoding the analogue when the temp. is increased such that the repressor is inactivated. The plasmid comprises 6 DNA sequences, an N-utilisation site and an ATG initiation codon.

USE/ADVANTAGE - Used for prodn. of polypeptide analogues of bovine growth hormone. Enhanced expression is possible, the vectors are stable and antibiotic resistance markers need not be used allowing cheaper prodn.

L21: Entry 15 of 21

File: DWPI

Oct 28, 1999

DERWENT-ACC-NO: 1992-143149

DERWENT-WEEK: 199951

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Human copper-zinc super oxide dismutase polypeptide analogue prodn. - by culturing transformed bacterial cells in zinc-contg. prodn. medium contg. copper ions for ischaemia treatment

ABTX :

Prodn. comprises (a) growing a culture of bacterial cells in a zinc-contg. prodn. medium supplemented with a non-growth inhibiting amt. of Cu<sup>2+</sup> so final concn. of Cu<sup>2+</sup> in the medium is more than 2 ppm, where the cells contain and express DNA encoding the polypeptide analogue of human Cu/Zn SOD and where the culture is grown under pref. conditions to express DNA and produce polypeptide in the bacterial cells and (b) recovering obtd. enzymatically active analogue of human Cu/Zn SOD etc.

ABEQ:

Prodn. comprises (a) growing a culture of bacterial cells in a zinc-contg. prodn. medium supplemented with a non-growth inhibiting amt. of Cu<sup>2+</sup> so final concn. of Cu<sup>2+</sup> in the medium is more than 2 ppm, where the cells contain and express DNA encoding the polypeptide analogue of human Cu/Zn SOD and where the culture is grown under pref. conditions to express DNA and produce polypeptide in the bacterial cells and (b) recovering obtd. enzymatically active analogue of human Cu/Zn SOD etc.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KWD](#) | [Draw Desc](#) | [Image](#)

---

16. Document ID: GB 2221907 A, AU 8937888 A, DE 68900915 E, EP 355348 A, EP 355348 B, EP 355348 B2, ES 2014764 A, FR 2634125 A, GB 2221907 B, IT 1231473 B, JP 02022233 A, JP 94010138 B2, US 4966774 A

L21: Entry 16 of 21

File: DWPI

Feb 21, 1990

DERWENT-ACC-NO: 1990-053069

DERWENT-WEEK: 199008

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Compsn. used as antiinflammatory agent - comprises super:oxide:dismutase, phosphate, alkali metal chloride and sucrose

INVENTOR: KATOH, K; NAKANO, M ; KATCH, K

PRIORITY-DATA: 1988JP-0171794 (July 12, 1988)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
GB 2221907 A	February 21, 1990		014	
AU 8937888 A	January 18, 1990		000	
DE 68900915 E	April 9, 1992		000	
EP 355348 A	February 28, 1990	E	000	
EP 355348 B	March 4, 1992		000	
EP 355348 B2	June 22, 1994	E	006	A61K037/50
ES 2014764 A	July 16, 1990		000	
FR 2634125 A	January 19, 1990		000	
GB 2221907 B	October 9, 1991		000	
IT 1231473 B	December 7, 1991		000	A61K000/00
JP 02022233 A	January 25, 1990		000	
JP 94010138 B2	February 9, 1994		003	A61K037/50
US 4966774 A	October 30, 1990		000	

INT-CL (IPC): A61K 31/70; A61K 33/42; A61K 35/50; A61K 37/50; A61K 47/02; A61K 47/24; A61K 47/26; C12N 9/08

ABSTRACTED-PUB-NO: GB 2221907A

BASIC-ABSTRACT:

A compsn. comprises a superoxide dismutase (SOD), a phosphate, an alkali metal chloride and sucrose.

The SOD may be of the Cu-Zn, Fe, Mn type of SOD. E.g. are a Cu-Zn, SOD originating from plants such as spinach, an Mn SOD originating from bacteria such as E. coli or SODs prep'd. by genetic recombination techniques. Pref. human Cu-Zn SOD is used. The alkali metal chloride may be e.g. KCl, pref. NaCl. Pref. the phosphate is inorganic such as an alkali metal phosphate esp. Na phosphate. Pref. amts. used per 100000 U of SOD protein are 0.05-50, esp. 0.1-25 mg. of alkali metal chloride, 0.05-20, esp. 0.3-4 micro-mol., of phosphate (as phosphoric acid) and 1-150 esp. 7-60 mg. of sucrose. Other additives, such as fillers and adjuvants, may be present in an amt. e.g. of up to 5 g. The compsn. may be for oral, injection or external use.

USE/ADVANTAGE - SOD is used in the prevention and treatment of tissue disorders caused by superoxides and may be employed e.g. as an antiinflammatory agent or a remedy for ischemic cardiac diseases. It is advantageous to use purified SODs, partic. human Cu-Zn SOD, because bovine SOD shows an antigenicity when administered to man.

ABSTRACTED-PUB-NO:

DE 8900915E EQUIVALENT-ABSTRACTS:

A compsn. comprises a superoxide dismutase (SOD), a phosphate, an alkali metal chloride and sucrose. The SOD may be of the Cu-Zn, Fe, Mn type of SOD. E.g. are a Cu-Zn, SOD originating from plants such as spinach, an Mn SOD originating from bacteria such as E. coli or SODs prep'd. by genetic recombination techniques. Pref. human Cu-Zn SOD is used. The alkali metal chloride may be e.g. KCl, pref. NaCl. Pref. the phosphate is inorganic such as an alkali metal phosphate esp.

Na phosphate. Pref. amts. used per 100000 U of SOD protein are 0.05-50, esp. 0.1-25 mg. of alkali metal chloride, 0.05-20, esp. 0.3-4 micro-mol., of phosphate (as phosphoric acid) and 1-150 esp. 7-60 mg. of sucrose. Other additives, such as fillers and adjuvants, may be present in an amt. e.g. of up to 5 g. The compsn. may be for oral, injection or external use. USE/ADVANTAGE - SOD is used in the prevention and treatment of tissue disorders caused by superoxides and may be employed e.g. as an antiinflammatory agent or a remedy for ischemic cardiac diseases. It is advantageous to use purified SODs, partic. human Cu-Zn SOD, because bovine SOD shows an antigenicity when administered to man.

()

EP 355348B

A superoxide dismutase (SOD) composition comprising a phosphate, an alkali metal chloride and sucrose.

(7pp)

GB 2221907B

A composition comprising a superoxide dismutase (SOD) a phosphate, an alkali metal chloride and sucrose.

US 4966774A

Superoxide dismutase compsn. comprises superoxide dismutase (e.g. protein obtd. by recombinant DNA methods from human sources; 100,000 int. units); alkali metal chloride (about 0.05-50 mg.); alkali metal phosphate (about 0.05-20 micro-mol.); sucrose (about 1-150 mg.); and opt. additives and/or carriers (0-5g). USE - The prods. are stable preps. for the treatment of tissue disorders arising from superoxides, e.g. inflammation, ischemic cardiac disease, rheumatoid arthritis, etc., without antigenic side effects.

(4pp)

L21: Entry 16 of 21

File: DWPI

Feb 21, 1990

DERWENT-ACC-NO: 1990-053069

DERWENT-WEEK: 199008

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Compsn. used as antiinflammatory agent - comprises super:oxide:dismutase, phosphate, alkali metal chloride and sucrose

ABTX:

The SOD may be of the Cu-Zn, Fe, Mn type of SOD. E.g. are a Cu-Zn, SOD originating from plants such as spinach, an Mn SOD originating from bacteria such as E. coli or SODs prep'd. by genetic recombination techniques. Pref. human Cu-Zn SOD is used. The alkali metal chloride may be e.g. KCl, pref. NaCl. Pref. the phosphate is inorganic such as an alkali metal phosphate esp. Na phosphate. Pref. amts. used per 100000 U of SOD protein are 0.05-50, esp. 0.1-25 mg. of alkali metal chloride, 0.05-20, esp. 0.3-4 micro-mol., of phosphate (as phosphoric acid) and 1-150 esp. 7-60 mg. of sucrose. Other additives, such as fillers and adjuvants, may be present in an amt. e.g. of up to 5 g. The compsn. may be for oral, injection or external use.

ABEQ:

A compsn. comprises a superoxide dismutase (SOD), a phosphate, an alkali metal chloride and sucrose. The SOD may be of the Cu-Zn, Fe, Mn type of SOD. E.g. are a Cu-Zn, SOD originating from plants such as spinach, an Mn SOD originating from bacteria such as E. coli or SODs prep'd. by genetic recombination techniques. Pref. human Cu-Zn SOD is used. The alkali metal chloride may be e.g. KCl, pref. NaCl. Pref. the phosphate is inorganic such as an alkali metal phosphate esp.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KUMC](#) | [Drawn Desc](#) | [Image](#)

17. Document ID: EP 349113 A, JP 2567664 B2, JP 01299300 A, JP 02025750 A, JP 02231568 A, JP 02232562 A, CN 1040821 A, US 5147783 A, EP 349113 B1, DE 68921374 E

L21: Entry 17 of 21

File: DWPI

Jan 3, 1990

DERWENT-ACC-NO: 1990-009116

DERWENT-WEEK: 199705

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Monoclonal antibody against human manganese-super-oxide dismutase - useful in diagnostic assays for epithelial ovarian cancer and myocardial infarction

INVENTOR: HIFUMI, E; ISHIKAWA, M ; ITOH, Y ; KAWAGUCHI, T ; NOJI, S ; SUZUKI, K ; TANIGUCHI, N ; UDA, T

PRIORITY-DATA: 1989JP-0052780 (March 7, 1989), 1988JP-0128165 (May 27, 1988), 1988JP-0175129 (July 15, 1988), 1989JP-0050005 (March 3, 1989)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
EP 349113 A	January 3, 1990	E	000	
JP 2567664 B2	December 25, 1996		007	C12P021/08
JP 01299300 A	December 4, 1989		000	
JP 02025750 A	January 29, 1990		000	
JP 02231568 A	September 13, 1990		000	
JP 02232562 A	September 14, 1990		000	
CN 1040821 A	March 28, 1990		000	
US 5147783 A	September 15, 1992		029	G01N033/543
EP 349113 B1	March 1, 1995	E	039	C12P021/08
DE 68921374 E	April 6, 1995		000	C12P021/08

INT-CL (IPC): A61K 39/395; C07K 16/40; C12N 5/10; C12N 5/18; C12N 15/00; C12N 15/02; C12P 21/00; C12P 21/08; G01N 33/54 ; G01N 33/543; G01N 33/573; G01N 33/574; G01N 33/577; G01N 33/58; C12P 21/08; C12R 1/91

ABSTRACTED-PUB-NO: EP 349113A

BASIC-ABSTRACT:

Monoclonal antibody (I) against human manganese-superoxide dismutase (SOD) is produced by a cell line obtd. by fusion of lymphocytes from a mouse immunised with human Mn-SOD and mouse myeloma cells. (I) has high specificity against human Mn-SOD. Kit for assaying human Mn-SOD contains (I) and enzyme-labelled (I).

(I) is obtd. from one of the following cell lines: N18 (FERM-P No. 1606), PE9 (FERM-P No. 1607), or P6 11 (FERM P No. 1608).

USE/ADVANTAGE - (I) is useful for assaying human Mn-SOD in diagnosis of human epithelial ovarian cancer and myocardial infarction (methods claimed). The diagnostic assays are easy to perform and highly sensitive. The positive ratio and specificity are also good. The diagnosis of myocardial infarction using (I) is advantageous over prior art methods as frequent blood sampling is not required, and it is not affected by reperfusion after therapy of myocardial infarction.

ABSTRACTED-PUB-NO:

EP 349113B EQUIVALENT-ABSTRACTS:

Monoclonal antibodies to human manganese superoxide dismutase (human Mn-SOD) obtainable from the hybridoma strains deposited at the Fermentation Research Institute Agency of Industrial Science and Technology and having the accession numbers FERM-BP 1606, FERM-BP 1607 and FERM-BP 1608.

US 5147783A

Process for screening for human epithelial ovarian cancer comprises determination of human manganese superoxide dismutase in a body fluid sample by incubation with

monoclonal antibody immobilised on a solid carrier; sepn. of the solid and soln. phases; and measurement of the extent of complex formation (a concn. 130 ng/cm<sup>3</sup> or more of the dismutase is positive). Monoclonal antibody against human manganese superoxide dismutase (which is not reactive with human alubmin, globulin, or Cu or Zn superoxide dismutases) is obtd. from a cell line produced by immunisation of mice with this dismutase and then fusion of the mouse lymphocytes with mouse myeloma cells. ADVANTAGE - Sample can be assayed rapidly and with high sensitivity.

L21: Entry 17 of 21

File: DWPI

Jan 3, 1990

DERWENT-ACC-NO: 1990-009116

DERWENT-WEEK: 199705

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Monoclonal antibody against human manganese-super-oxide dismutase - useful in diagnostic assays for epithelial ovarian cancer and myocardial infarction

## ABTX:

Monoclonal antibody (I) against human manganese-superoxide dismutase (SOD) is produced by a cell line obtd. by fusion of lymphocytes from a mouse immunised with human Mn-SOD and mouse myeloma cells. (I) has high specificity against human Mn-SOD. Kit for assaying human Mn-SOD contains (I) and enzyme-labelled (I).

## ABEQ:

Process for screening for human epithelial ovarian cancer comprises determination of human manganese superoxide dismutase in a body fluid sample by incubation with monoclonal antibody immobilised on a solid carrier; sepn. of the solid and soln. phases; and measurement of the extent of complex formation (a concn. 130 ng/cm<sup>3</sup> or more of the dismutase is positive). Monoclonal antibody against human manganese superoxide dismutase (which is not reactive with human alubmin, globulin, or Cu or Zn superoxide dismutases) is obtd. from a cell line produced by immunisation of mice with this dismutase and then fusion of the mouse lymphocytes with mouse myeloma cells. ADVANTAGE - Sample can be assayed rapidly and with high sensitivity.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)[KwIC](#) | [Draw Desc](#) | [Image](#) 18. Document ID: JP 63209584 A, JP 94053068 B2

L21: Entry 18 of 21

File: DWPI

Aug 31, 1988

DERWENT-ACC-NO: 1988-288416

DERWENT-WEEK: 198841

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Prodn. of copper and zinc coordinated superoxidizedismutase - by putting cultured bacteria of SOD-producing recombinant microorganisms in buffer soln. contg. copper and zinc salts

PRIORITY-DATA: 1987JP-0042801 (February 27, 1987)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 63209584 A	August 31, 1988		006	
JP 94053068 B2	July 20, 1994		004	C12N009/02

INT-CL (IPC): C12N 1/06; C12N 9/02; C12N 15/00; C12R 1/19; C12N 9/02; C12R 1/19

ABSTRACTED-PUB-NO: JP63209584A

BASIC-ABSTRACT:

Prodn. comprises crashing cultured bacterial bodies of recombinant microorganisms capable of producing superoxide dismutase in a buffer soln. contg. a water-sol. copper salt and zinc salt to form copper and zinc coordinated superoxide dismutase and collecting it.

Water-sol. copper salts used are not limited to any kinds as far as they dissociate into copper ions in a buffer soln., but usually copper salts of strong acid are employed, e.g. copper sulphate, copper nitrate, and copper hydrochloride; copper sulphate is most pref. As water-sol. zinc salts, those which dissociate themselves into zinc ions in a buffer soln. may be used, e.g. zinc sulphate, zinc nitrate, zinc hydrochloride; zinc sulphate is most pref. The density of the water-sol. salt in the buffer soln. may be fixed by specifying the number of microorganisms and the prodn. amt. of superoxide dismutase. Each of the densities of water-sol. copper and zinc salts are 0.03-20 mM, pref. 0.5-10 mM when 10 power (13) of microorganisms are suspended in 1 ml of the buffer soln. The buffer soln. used is pref. 50 mm tris-HCl (pH 7.5).

USE/ADVANTAGE - Copper and zinc are quantitatively coordinated by gene engineering. Copper and zinc coordinated superoxide dismutase may be applied to the treatment of inflammation by active oxygen, e.g. osteoarthritis, chronic rheumatism, radiation disturbances, etc.

L21: Entry 18 of 21

File: DWPI

Aug 31, 1988

DERWENT-ACC-NO: 1988-288416

DERWENT-WEEK: 198841

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Prodn. of copper and zinc coordinated superoxidizedismutase - by putting cultured bacteria of SOD-producing recombinant microorganisms in buffer soln. contg. copper and zinc salts

ABTX:

Prod n. comprises crashing cultured bacterial bodies of recombinant microorganisms capable of producing superoxide dismutase in a buffer soln. contg. a water-sol. copper salt and zinc salt to form copper and zinc coordinated superoxide dismutase and collecting it.

TTX:

PRODUCE COPPER ZINC COORDINATE SUPEROXIDEDISMUTASE PUTTING CULTURE BACTERIA SOD  
PRODUCE RECOMBINATION MICROORGANISM BUFFER SOLUTION CONTAIN COPPER ZINC SALT

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)[KMC](#) | [Draw Desc](#) | [Image](#) 19. Document ID: JP 61212600 A

L21: Entry 19 of 21

File: DWPI

Sep 20, 1986

DERWENT-ACC-NO: 1986-289075

DERWENT-WEEK: 198644

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Monoclonal antibody for human copper, zinc super-oxide dismutase - by preparing myeloma cells and fusing with immunised lymphocytes, blending, incubating, cloning and culturing

PRIORITY-DATA: 1985JP-0053485 (March 19, 1985)

## PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 61212600 A	September 20, 1986		007	

INT-CL (IPC): A61K 39/39; C07K 15/04; C12N 15/00

ABSTRACTED-PUB-NO: JP61212600A

## BASIC-ABSTRACT:

Anti-human Cu, Zn-superoxide dismutase (Cu, Zn-SOD)-monoclonal antibody having a specificity to human Cu, Zn-SOD.

Anti-human Cu, Zn-SOD-monoclonal antibody can be obtd. by incubation of anti-human Cu, Zn-SOD-monoclonal antibody-producing hybridoma cell strain. (a) A mouse or rat is immunised with human Cu, Zn-SOD antigen, and the lymphocytes of the immunized animal are taken out from the spleen and used for the cell fusion in the next step. (b) Mouse-derived P3U1, MS-1 or SP2/0 can be used as the myeloma cells. These myeloma cells are pref. incubated in 8-AG medium for 8-AG-sensitivity back-mutation. (c) The lymphocytes from the immunized animal (step (A)) and the myeloma cells (step (b)) were blended in MEM (Eagle MEM RTM) medium in a ratio of (5-10):1 in the presence of PEG (average molecular wt. 1,000-8,000 at a concn. of 30-60%) for cell fusion. (d) After cell fusion, the cells were incubated in normal HAT medium for the selection of hybridoma. The incubation was carried out for about several days, and the selected hybridoma are incubated in HT medium (contg. hypoxanthin and thymidine). (e) The determin. as to whether or not the selected hybridoma can actually produce anti-human Cu, Zn-SOD-antibody is carried out by conventional ELISA method (enzyme-immunoassay). (f) The anti-human Cu, Zn-SOD-antibody-producing hybridoma as selected is cloned in single cell manipulation method, and a clone having higher specificity to the aimed antigen is selected. (g) The clone as selected in the step (f) is used for the prodn. of the desired monoclonal antibody in an abdomen of test animals or by tissue-culture. The monoclonal antibody thus produced has a specificity to human Cu, Zn-SOD.

USE/ADVANTAGE - Useful for the measurement of human Cu, Zn-SOD and is therefore useful for the diagnosis of uremia. Anti-human Cu, Zn-SOD-mono clonal antibody can be obtd. by incubation of anti-human Cu, Zn-SOD-monoclonal antibody-producing hybridoma cell strain.

L21: Entry 19 of 21

File: DWPI

Sep 20, 1986

DERWENT-ACC-NO: 1986-289075

DERWENT-WEEK: 198644

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Monoclonal antibody for human copper, zinc super-oxide dismutase - by preparing myeloma cells and fusing with immunised lymphocytes, blending, incubating, cloning and culturing

ABTX:

Anti-hu man Cu, Zn-superoxide dismutase (Cu, Zn-SOD)-monoclonal antibody having a specificity to human Cu, Zn-SOD.

ABTX:

Anti-human Cu, Zn-SOD-monoclonal antibody can be obtd. by incubation of anti-human Cu, Zn-SOD-monoclonal antibody-producing hybridoma cell strain. (a) A mouse or rat is immunised with human Cu, Zn-SOD antigen, and the lymphocytes of the immunized animal are taken out from the spleen and used for the cell fusion in the next step. (b) Mouse-derived P3U1, MS-1 or SP2/0 can be used as the myeloma cells. These myeloma cells are pref. incubated in 8-AG medium for 8-AG-sensitivity back-mutation. (c) The lymphocytes from the immunized animal (step (A)) and the myeloma cells (step (b)) were blended in MEM (Eagle MEM RTM) medium in a ratio of (5-10):1 in the presence of PEG (average molecular wt. 1,000-8,000 at a concn. of 30-60%) for cell fusion. (d) After cell fusion, the cells were incubated in normal HAT medium for the selection of hybridoma. The incubation was carried out for about several days, and the selected hybridoma are incubated in HT medium (contg. hypoxanthin and thymidine). (e) The determin. as to whether or not the selected hybridoma can actually produce anti-human Cu, Zn-SOD-antibody is carried out by conventional ELISA method (enzyme-immunoassay). (f) The anti-human Cu, Zn-SOD-antibody-producing hybridoma as selected is cloned in single cell manipulation method, and a clone having higher specificity to the aimed antigen is selected. (g) The clone as selected in the step (f) is used for the prodn. of the desired monoclonal antibody in an abdomen of test animals or by tissue-culture. The monoclonal antibody thus produced has a specificity to human Cu, Zn-SOD.

ABTX:

USE/ADVANTAGE - Useful for the measurement of human Cu, Zn-SOD and is therefore useful for the diagnosis of uremia. Anti-human Cu, Zn-SOD-mono clonal antibody can be obtd. by incubation of anti-human Cu, Zn-SOD-monoclonal antibody-producing hybridoma cell strain.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMC](#) | [Draw Desc](#) | [Image](#)

20. Document ID: CA 1340597 C, EP 173280 A, PT 81025 A, AU 8546677 A, ZA 8506468 A, JP 61111693 A, DK 8503841 A, ES 8700321 A, HU 40697 T, ES 8704208 A, ES 8704209 A, DD 251787 A, US 4742004 A, AU 9060198 A, US 5059529 A, US 5081020 A, US 5112744 A, EP 173280 B1, DE 3586473 G, US 5151364 A, AU 9463099 A, JP 07222596 A, JP 07236490 A, SG 9590832 A, US 5527691 A, AU 671728 B, JP 08283296 A, IL 108976 A, IL 110039 A, IL 76192 A, JP 2688180 B2, JP 2777074 B2, HU 214977 B, HU 215160 B, CA 1340464 C, JP 2933280 B2

L21: Entry 20 of 21

File: DWPI

Jun 22, 1999

DERWENT-ACC-NO: 1986-063162

DERWENT-WEEK: 199944

COPYRIGHT 2001 DERWENT INFORMATION LTD

**TITLE:** New expression vectors contg. lambda p1 promoter - with engineered restriction site for replacing ribosomal binding site to improve expression of enzymes, hormones etc.

**INVENTOR:** AVIV, H; BARTFELD, D ; GORECKI, M ; HARTMAN, J R ; KANNER, D ; LEVANON, A ; LOCKER-GILADI, H ; OPPENHEIM, A B ; LOCKERGILA, H ; OPPERNHEIM, A B ; LOCKER-GALADI, H ; VOGEL, T

**PRIORITY-DATA:** 1984US-0645119 (August 27, 1984), 1984US-0644105 (August 27, 1984), 1984US-0644245 (August 27, 1984), 1984US-0644551 (August 27, 1984), 1984US-0644671 (August 27, 1984), 1989US-0317629 (March 1, 1989), 1988US-0220783 (July 18, 1988), 1988US-0155111 (February 11, 1988), 1990US-0539367 (June 15, 1990), 1992US-0822054 (January 14, 1992), 1989US-0317434 (March 1, 1989), 1992US-0893076 (June 3, 1992), 1994US-0267794 (June 28, 1994)

**PATENT-FAMILY:**

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
CA 1340597 C	June 22, 1999	E	000	C12N015/73
EP 173280 A	March 5, 1986	E	252	
PT 81025 A	February 10, 1986		000	
AU 8546677 A	March 6, 1986		000	
ZA 8506468 A	March 13, 1986		000	
JP 61111693 A	May 29, 1986		000	
DK 8503841 A	February 28, 1986		000	
ES 8700321 A	January 1, 1987		000	
HU 40697 T	January 28, 1987		000	
ES 8704208 A	June 1, 1987		000	
ES 8704209 A	June 1, 1987		000	
DD 251787 A	November 25, 1987		000	
US 4742004 A	May 3, 1988		000	
AU 9060198 A	November 8, 1990		000	
US 5059529 A	October 22, 1991		034	
US 5081020 A	January 14, 1992		037	
US 5112744 A	May 12, 1992		039	C12N015/00
EP 173280 B1	August 12, 1992	E	126	C12N015/73
DE 3586473 G	September 17, 1992		000	C12N015/73
US 5151364 A	September 29, 1992		036	C12N015/70
AU 9463099 A	July 28, 1994		000	C12N015/53
JP 07222596 A	August 22, 1995		070	C12P021/02
JP 07236490 A	September 12, 1995		070	C12N015/09
SG 9590832 A	December 22, 1995		000	
US 5527691 A	June 18, 1996		038	C12N001/21
AU 671728 B	September 5, 1996		000	C12N015/53
JP 08283296 A	October 29, 1996		068	C07K014/775
IL 108976 A	December 5, 1996		000	C12N015/73
IL 110039 A	December 5, 1996		000	C12P021/00
IL 76192 A	December 5, 1996		000	C12P021/02
JP 2688180 B2	December 8, 1997		068	C12N015/09
JP 2777074 B2	July 16, 1998		071	C12N015/09
HU 214977 B	August 28, 1998		000	C12N015/73
HU 215160 B	October 28, 1998		000	C12N015/53
CA 1340464 C	March 23, 1999		000	C12N009/02
JP 2933280 B2	August 9, 1999		092	C12N015/00

A INT-CL (IPC): A01N 1/02; A61K 35/74; A61K 37/50; A61K 38/00; A61K 38/27; A61K 38/44; C07G 17/00; C07H 21/04; C07K 1/14; C07K 13/00; C07K 14/61; C07K 14/775; C07K 15/12; C12N 1/20; C12N 1/21; C12N 9/02; C12N 9/08; C12N 15/00; C12N 15/09; C12N 15/18; C12N 15/53; C12N 15/67; C12N 15/70; C12N 15/73; C12P 3/00; C12P 7/00; C12P 19/34; C12P 21/00; C12P 21/02; C12R 1/19; C12N 9/02; C12R 1/19; C12P 21/02; C12R 1/19; C12P 21/02; C12R 1/19; C12N 9/02; C12R 1/19; C12P 21/02; C12R 1/19

ABSTRACTED-PUB-NO: EP 173280A

BASIC-ABSTRACT:

(1) Vector that on introduction into a suitable bacterial host cell contg. the thermolabile repressor C (I) renders the host cell capable, when the temp. is raised to a level at which the repressor is inactivated, of effecting expression of a desired gene inserted in the vector to produce polypeptide (I) encoded by the gene is new when it comprises a double-stranded DNA molecule including in 5'-to 3' - order.

(a) DNA sequence contg. the promoter and operator P(L)O(L) from lambda bacteriophage; (b) a N utilisation site for binding antiterminator N protein; (c) a first restriction enzyme site permitting replacement of the DNA sequence contg. the ribosomal binding site following after; (d) DNA sequence contg. a ribosomal binding site for making the mRNA of the desired gene capable of binding to ribosomes in the host cell; (e) ATG initiator codon or a DNA sequence converted into the codon on insertion of the desired gene into the vector; and (f) a second restriction enzyme site for inserting the desired gene into the vector in phase with the ATG initiation codon; and (g) a DNA sequence contg. an origin of replication from a bacterial plasmid capable of autonomous replication in the host cell; and for selection, DNA sequence contg. a gene associated with a selectable or identifiable phenotypic trait manifested when the vector is present in the host cell, or DNA sequence contg. fragment C (I) 434, including the gene for the C (I) 434 repressor protein and its associated promoter and operator sequence.

USE/ADVANTAGE - The expression vectors provide enhanced expression of various polypeptides, esp. when different ribosomal binding sites are used. The transcription termination sequences permit origins of replication from high copy number plasmids to be incorporated.

ABSTRACTED-PUB-NO:

US 4742004A EQUIVALENT-ABSTRACTS:

An enzymatically active polypeptide analogue of human Cu/Zn superoxide dismutase (CSD) is produced by growing a culture of bacterial cells, pref. E coli, in a prodn. medium contg. Zn and at least 2 ppm Cu but not a growth inhibitory amount. The cells contain and are able to express DNA encoding the polypeptide analogue of human CSD. The culture is grown under such conditions that the DNA is expressed and the polypeptide is grown in the cells. The culture of the bacterial cells pref. has been transformed with a plasmid contg. incorporated the DNA sequence encoding the polypeptide analogue of human CSD. The prodn. medium contains esp. 75 ppm Cu<sup>2+</sup> and at least 2ppm Zn. The CSD is recovered and purified by (a) disrupting the isolated cells, (b) separating the cell debris from the soluble protein supernatant soln. and heating the soln. for 2 hrs to 65 deg.C, (c) cooling the soln. and separating from it a clear supernatant protein soln. contg. the analogue and recovering it from the soln.

USE/ADVANTAGE - Opt. e.g. prevention o+ oncogenesis, reducing the cytotoxic and cardiotoxic effects of anticancer drugs; to study the ageing process; the analogue contains the same amino acid sequence and has the same activity as naturally occurring CSD. (34pp)o

US 5059529A

Plasmid pHG50 (ATCC 39805) is a new expression vector that controls the prodn. of a polypeptide analogue of bovine growth hormone. Prodn. of this polypeptide

comprises transforming a suitable host microorganism, e.g. Escherichia coli (strain A1645, lambda-i-434cI-mini Tn 10), propagation of the transformed cells, and isolation and purification of the polypeptide.

USE - The prodn. is a valuable growth stimulant. (34pp) o

US 5081020A

Plasmid p8300-10A (ATCC 39785) transforms host cells (e.g. Escherichia coli) to produce a bovine growth hormone polypeptide analogue in which a Met unit is attached to the N-terminal Phe gp. of the naturally occurring polypeptide, without loss of biologically activity. Other plasmids (e.g. pSAL-130/5 and -170/10) lead to the prodn. of growth hormone analogues in which Met, Asp and Glu are attached to the N-terminal Phe gp., without loss of biological activity.

USE - The transformed cells are propagated to produce these bovine growth hormone analogues. (37pp)

US 5112744A

Plasmids and expression vectors that encode the prodn. of polypeptides, one apparently identical to human Cu-Zn superoxide dismutase, "pSOD-beta1-TT-1", are new. Prodн. of this enzyme comprises transforming suitable host cells, e.g. Escherichia coli A-1645, with the above expression vectors; propagation of the transformed species; isolation of the polypeptide; and purifcn.

USE - This and other biologically active polypeptides (e.g. apolipoprotein -E) facilitate biochemical synthesis or analysis and provide valuable diagnostic reagents and therapeutics.e

US 5126252A

Plasmid for the prodn. of bovine or porcine growth hormone or their active polypeptide fragments or analogues comprises a double stranded DNA contg. in the order 5' to 3' a promoter PLOL (from a lambda-bacteriophage); a single N-utilisation site for binding non-terminal protein NutL; a sequence TAAGGAAGTACTTACATATTCTTCATGAATGTA contg. the mutant CII ribosomal binding site (from a lambda-bacteriophage); an NdeI restriction enzyme site including an ATG initiation codon; a sequence that encodes the prodn. of the growth hormone or its active fragments; sequence contg. a T1T2 rRNA transcription termination gp.; and an origin of replication (from the bacterial plasmid pBR322).

USE - Escherichia coli cells are transformed with these plasmids and propagated to produce bovine or porcine growth hormone or corresp. active fragments or analogues.s

US 5527691A

A plasmid for the production of human apolipoprotein E having substantially the same amino acid sequence as, and the biological activity of, the naturally occurring human apolipoprotein E, which plasmid upon introduction into a suitable Escherichia coli host cell containing the thermolabile repressor cI renders the host cell capable, upon increasing the temperature of the Escherichia coli host cell to a temperature at which the repressor is inactivated, of effecting expression of DNA encoding the apolipoprotein E, said plasmid comprising a double-stranded DNA molecule which includes in 5' to 3' order the following:

- (a) DNA which contains the promoter and operator PLOL from lambda bacteriophage;
- (b) a single N utilization site for binding antiterminator N protein produced by the Escherichia coli host cell, the site being NutL;
- (c) a DNA sequence containing the mutant CII ribosomal binding site from lambda bacteriophage having the sequence

5' TAAGGAAGTACTTACAT-3'

3' ATTCCCTTCATGAATGTAS';

(D) An NdeI restriction enzyme site including an ATG initiation codon;

e) DNA encoding the apolipoprotein E inserted into the NdeI restriction enzyme site in phase with the ATG initiation codon;

(f) a DNA sequence which contains a T1T2 rRNA transcription termination sequence located less than 100 base pairs from the DNA encoding the apolipoprotein E;

and which additionally includes a DNA sequence which contains an origin of replication from the bacterial plasmid pBR322 which is capable of autonomous replication in the Escherichia coli host cell and a DNA sequence which contains a gene associated with a selectable or identifiable phenotypic trait which is manifested when the plasmid is present in the Escherichia coli host cell, the distance between the 3' end of the P1OL promoter and operator sequence and the 5' end of the N utilization site being less than about 80 base pairs and the distance between the 3' end of the N utilization site and the 5' end of the ribosomal binding site being less than about 300 base pairs.

L21: Entry 20 of 21

File: DWPI

Jun 22, 1999

DERWENT-ACC-NO: 1986-063162

DERWENT-WEEK: 199944

COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: New expression vectors contg. lambda p1 promoter - with engineered restriction site for replacing ribosomal binding site to improve expression of enzymes, hormones etc.

ABEQ:

An enzymatically active polypeptide analogue of human Cu/Zn superoxide dismutase (CSD) is produced by growing a culture of bacterial cells, pref. E coli, in a prodn. medium contg. Zn and at least 2 ppm Cu but not a growth inhibitory amount. The cells contain and are able to express DNA encoding the polypeptide analogue of human CSD. The culture is grown under such conditions that the DNA is expressed and the polypeptide is grown in the cells. The culture of the bacterial cells pref. has been transformed with a plasmid contg. incorporated the DNA sequence encoding the polypeptide analogue of human CSD. The prodn. medium contains esp. 75 ppm Cu<sup>2+</sup> and at least 2ppm Zn. The CSD is recovered and purified by (a) disrupting the isolated cells, (b) separating the cell debris from the soluble protein supernatant soln. and heating the soln. for 2 hrs to 65 deg.C, (c) cooling the soln. and separating from it a clear supernatant protein soln. contg. the analogue and recovering it from the soln.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMC](#) | [Draw. Desc](#) | [Image](#)

21. Document ID: JP 57141288 A

L21: Entry 21 of 21

File: DWPI

Sep 1, 1982

DERWENT-ACC-NO: 1982-86446E  
DERWENT-WEEK: 198241  
COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Superoxidedismutase prodn. from human cells - using carrier to which is bound specific antibody for superoxidizedismutase, useful as antiinflamma tory

PRIORITY-DATA: 1981JP-0026730 (February 27, 1981)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 57141288 A	September 1, 1982		008	

INT-CL (IPC): C12N 9/00

ABSTRACTED-PUB-NO: JP57141288A

BASIC-ABSTRACT:

The process comprises using a carrier to which is bound a specific antibody for superoxide dismutase from human cells. Superoxide dysnutase (SOD) is a metalloprotein showing antiinflammatory activity. SOD obtained from human cells is non-toxic and non-antigenic. The LD<sub>50</sub> values of Mn-SOD and Cu, Zn-SOD in mice are at least 50 mg/kg and at least 70 mg/kg, respectively.

Cu, Zn-SOD and Mn-SOD can be prep'd by disrupting human cells (derived from liver, red cell, heart, kidney) in 1.15 % KCl, centrifuging the disrupted cells, heating the supernatant at 60-75 deg.C. cooling the soln, removing the ppt. and treating the supernatant with a carrier to which a specific antibody for SOD is bound. The carrier can be prep'd. by reacting a carrier (e.g. Sepharose 4 B) with SOD-antibody obtd. by immunisation of guinea pig with SOD and Freund's complete adjuvant. Such condensn. can be carried out by BrCN method.

L21: Entry 21 of 21

File: DWPI

Sep 1, 1982

DERWENT-ACC-NO: 1982-86446E  
DERWENT-WEEK: 198241  
COPYRIGHT 2001 DERWENT INFORMATION LTD

TITLE: Superoxidedismutase prodn. from human cells - using carrier to which is bound specific antibody for superoxidizedismutase, useful as antiinflamma tory

ABTX:

The process comprises using a carrier to which is bound a specific antibody for superoxide dismutase from human cells. Superoxide dysnutase (SOD) is a metalloprotein showing antiinflammatory activity. SOD obtained from human cells is non-toxic and non-antigenic. The LD<sub>50</sub> values of Mn-SOD and Cu, Zn-SOD in mice are at least 50 mg/kg and at least 70 mg/kg, respectively.

ABTX:

Cu, Zn-SOD and Mn-SOD can be prep'd by disrupting human cells (derived from liver, red cell, heart, kidney) in 1.15 % KCl, centrifuging the disrupted cells, heating the supernatant at 60-75 deg.C. cooling the soln, removing the ppt. and treating the supernatant with a carrier to which a specific antibody for SOD is bound. The carrier can be prep'd. by reacting a carrier (e.g. Sepharose 4 B) with SOD-antibody obtd. by immunisation of guinea pig with SOD and Freund's complete adjuvant. Such condensn. can be carried out by BrCN method.

Term	Documents
(20 NOT (12 OR 9 OR 6)).JPAB,EPAB,DWPI.	21

Documents, starting with Document:

Display Format:

**WEST**

# Freeform Search

**Database:**

US Patents Full-Text Database  
US Pre-Grant Publication Full-Text Database  
JPO Abstracts Database  
EPO Abstracts Database  
Derwent World Patents Index  
IBM Technical Disclosure Bulletins

**Term:****Display:** 25 **Documents in Display Format:** CIT **Starting with Number** 1**Generate:**  Hit List  Hit Count  Image

---

---

---

## Search History

---

**Today's Date:** 12/5/2001

<u>DB Name</u>	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u>
USPT,PGPB	superoxide dismutase or sod	4385	<u>L1</u>
USPT,PGPB	(copper zinc) or (cu zn) or cuprozinc or cuzn or cu/zn	15235	<u>L2</u>
USPT,PGPB	11 with 12	301	<u>L3</u>
USPT,PGPB	13 or cuznsod	311	<u>L4</u>
USPT,PGPB	vaccine or vaccinat\$	13635	<u>L5</u>
USPT,PGPB	14 same 15	2	<u>L6</u>
USPT,PGPB	immunis? or immuniz?	4726	<u>L7</u>
USPT,PGPB	immunis\$ or immuniz\$	19004	<u>L8</u>
USPT,PGPB	14 same 18	2	<u>L9</u>
USPT,PGPB	19 not 16	1	<u>L10</u>
USPT,PGPB	bacteri\$ or gram negative	115085	<u>L11</u>
USPT,PGPB	14 with 111	31	<u>L12</u>
USPT,PGPB	11 near3 human	389	<u>L13</u>
USPT,PGPB	112 not 113	5	<u>L14</u>
USPT,PGPB	meningococc\$ or meningitis or actinobacillus or pleuropneumoniae or pasteurellaceae or neisseria or haemophilus or salmonella or salmonellosis or escherichia	27159	<u>L15</u>
USPT,PGPB	11 same 115	99	<u>L16</u>
USPT,PGPB	14 same 115	25	<u>L17</u>
USPT,PGPB	117 and (115 or 18)	2	<u>L18</u>
USPT,PGPB	117 same (15 or 18)	0	<u>L19</u>
USPT,PGPB	115 same (15 or 18)	1724	<u>L20</u>
USPT,PGPB	120 and 14	6	<u>L21</u>
USPT,PGPB	121 not (12 or 13)	0	<u>L22</u>
USPT,PGPB	121 not (16 or 19 or 114)	5	<u>L23</u>

**WEST****Generate Collection****Search Results - Record(s) 1 through 2 of 2 returned.** **1. Document ID: US 6149920 A**

L6: Entry 1 of 2

File: USPT

Nov 21, 2000

US-PAT-NO: 6149920

DOCUMENT-IDENTIFIER: US 6149920 A

TITLE: Over-expressing homologous antigen vaccine and a method of making the same

DATE-ISSUED: November 21, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Boyle; Stephen M.	Blacksburg	VA		
Cravero; Silvio	Republica			ARX
Corbeil; Lynette	San Diego	CA		
Schurig; Gerhardt	Blacksburg	VA		
Sriranganathan; Nammalwar	Blacksburg	VA		
Vemulapalli; Ramesh	Blacksburg	VA		

US-CL-CURRENT: 424/252.1, 424/184.1, 424/200.1, 424/234.1, 424/248.1, 424/261.1,  
435/243, 435/252.3, 435/320.1, 435/69.1, 435/69.3

## ABSTRACT:

This invention relates to an over-expressing homologous antigen vaccine, a method of producing the same, and use of the vaccine for prophylaxis or treatment of vertebrates at risk of or suffering from disease caused by a pathogenic micro-organism. The vaccine is an attenuated or avirulent pathogenic micro-organism that over-expresses at least one homologous antigen encoded by at least one gene derived from the pathogenic micro-organism, and may also express a heterologous antigen.

23 Claims, 5 Drawing figures Exemplary Claim Number: 1

Number of Drawing Sheets: 4

L6: Entry 1 of 2

File: USPT

Nov 21, 2000

DOCUMENT-IDENTIFIER: US 6149920 A

TITLE: Over-expressing homologous antigen vaccine and a method of making the same

DEPR:

It is particularly advantageous that the vaccine be prepared with one or more of a Cu/Zn SOD gene, a GroES gene or a GroEL gene of *B. abortus* strain RB51. In particular, it is preferred that the above genes be obtained from a pUC19 genomic library of *B. abortus* strain 2308.

DEPR:

A vaccine produced according to the above specifications is particularly effective for prophylaxis or treatment of diseases such as Brucellosis. For example, an effective vaccine for prophylaxis or treatment of a bovine animal against Brucellosis according to the invention is an attenuated or avirulent derivative of *B. abortus* strain RB51 capable of over-expressing at least one homologous antigen. In particular, it is preferred that the antigen be encoded by one or more of a Cu/Zn SOD gene, a GroES gene or a GroEL gene, preferably selected from a pUC19 genomic library of *B. abortus* strain 2308. It is even more preferable that the attenuated or avirulent derivative also express a heterologous antigen capable of inducing protective immunity against *B. abortus*.

DEPR:

After 6 weeks of vaccination, serum was collected from 3 mice in each group for analysis of the humoral antibody response. These mice were euthanized and the lymphocytes harvested from their spleens were used to study the cell-mediated immune response. As shown in FIG. 3, mice vaccinated with strain RB51 developed antibodies to GroEL but did not develop antibodies to Cu/Zn SOD. In contrast, mice vaccinated with strain RB51SOD developed a strong antibody response to Cu/Zn SOD, and mice vaccinated with strain RB51GroESL developed a stronger antibody response to GroEL protein (FIG. 3) than that exhibited by strain RB51 vaccinated mice. These results indicate an enhanced antibody response by the OHAV.

CLPR:

5. The vaccine of claim 4, wherein the at least one gene is a Cu/Zn SOD gene.

CLPR:

6. The vaccine of claim 5, wherein the Cu/Zn SOD gene is obtained from a pUC19 genomic library of *B. abortus* strain 2308.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Claims](#) | [KWMC](#) | [Draw Desc](#) | [Image](#)

---

2. Document ID: US 5188936 A

L6: Entry 2 of 2

File: USPT

Feb 23, 1993

US-PAT-NO: 5188936  
DOCUMENT-IDENTIFIER: US 5188936 A  
TITLE: Brucella abortus antibody detection methods  
DATE-ISSUED: February 23, 1993

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tabatabai; Louisa B.	Ames	IA		
Mayfield; John E.	Ames	IA		
Beck; Bonnie L.	Waterbury	CT		

US-CL-CURRENT: 435/7.32; 435/174, 435/189, 435/7.4

## ABSTRACT:

Diagnostic reagents comprising the 20 kd Brucella abortus CuZn superoxide dismutase (B. abortus 1CuZnSOD) protein and peptide segments thereof, which are effective as antigenic determinants, have been identified. These reagents are useful for detecting an antibody response to the B. abortus CuZnSOD protein in bovine serum or other body fluid samples and can also be used for distinguishing between animals which have serum antibody of a natural B. abortus infection and those which have an antibody response to a B. abortus Strain 19 vaccine or a B. abortus Strain which does not express the 20 kd protein.

7 Claims, 4 Drawing figures Exemplary Claim Number: 1  
Number of Drawing Sheets: 4

L6: Entry 2 of 2

File: USPT

Feb 23, 1993

DOCUMENT-IDENTIFIER: US 5188936 A  
TITLE: Brucella abortus antibody detection methods

## ABPL:

Diagnostic reagents comprising the 20 kd Brucella abortus CuZn superoxide dismutase (B. abortus 1CuZnSOD) protein and peptide segments thereof, which are effective as antigenic determinants, have been identified. These reagents are useful for detecting an antibody response to the B. abortus CuZnSOD protein in bovine serum or other body fluid samples and can also be used for distinguishing between animals which have serum antibody of a natural B. abortus infection and those which have an antibody response to a B. abortus Strain 19 vaccine or a B. abortus Strain which does not express the 20 kd protein.

## BSPR:

If cattle have been vaccinated with the vaccine strain of B. abortus or vaccinated with a mutant strain of B. abortus which does not express the CuZnSOD protein, the diagnostic reagents of the invention are also useful for distinguishing between animals which had a natural infection and those which have been vaccinated.

## DEPR:

As shown in FIG. 4, the CuZnSOD protein detects B. abortus-infected animals equally well as the PCFIA and RIV tests. Even though the agglutination tests (BAPA, Card, SPT, STT) detect a higher percentage of animals, these tests cannot always distinguish titers due to vaccination from infection. The CF test is sensitive and specific, but is cumbersome.

---

---

Term	Documents
(4 SAME 5).USPT,PGPB.	2

---

Documents, starting with Document:

**Display Format:**

**WEST****Generate Collection****Search Results - Record(s) 1 through 1 of 1 returned.** **1. Document ID: US 5147783 A**

L10: Entry 1 of 1

File: USPT

Sep 15, 1992

US-PAT-NO: 5147783

DOCUMENT-IDENTIFIER: US 5147783 A

TITLE: Methods to screen for ovarian cancer and myocardial infarction

DATE-ISSUED: September 15, 1992

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Uda; Taizo	Ube			JPX
Itoh; Yukikatsu	Ube			JPX
Kawaguchi; Tetsuo	Ube			JPX
Hifumi; Emi	Ube			JPX
Taniguchi; Naoyuki	Toyonaka			JPX
Suzuki; Keichiro	Takatsuki			JPX
Ishikawa; Mutsuo	Asahikawa			JPX
Noji; Shirou	Tokyo			JPX

US-CL-CURRENT: 435/7.23; 435/7.4, 436/518, 436/548, 436/813, 530/388.26

## ABSTRACT:

A monoclonal antibody against human manganese-superoxide dismutase characterized in that it is produced by a cell line which has been obtained by immunization of a mouse with human Mn-SOD and then fusion of lymphocytes obtained from the mouse with mouse myeloma cells, and has high specificity against human Mn-SOD; a method for producing a monoclonal antibody against human Mn-SOD having high specificity against human Mn-SOD, which comprises culturing the cell line obtained by immunization of a mouse with human Mn-SOD and then cell fusion of lymphocytes obtained from the mouse with mouse myeloma cells; a kit for assaying human Mn-SOD, comprising:

(a) a monoclonal antibody having very high specific immuno-reactivity against human Mn-SOD; and

(b) a reagent of a monoclonal antibody having very high specific immuno-reactivity against human Mn-SOD labelled with an enzyme (enzyme labelled antibody); a method for assaying human Mn-SOD use of the kit; a novel diagnostic method of human epithelial ovarian cancer, which comprises assaying the concentration of human Mn-SOD in a body fluid by use of the assay kit; and a novel diagnostic method of myocardial infarction, which comprises assaying the concentration of human Mn-SOD in a body fluid by use of the assay kit.

4 Claims, 16 Drawing figures Exemplary Claim Number: 1  
Number of Drawing Sheets: 16

L10: Entry 1 of 1

File: USPT

Sep 15, 1992

DOCUMENT-IDENTIFIER: US 5147783 A

TITLE: Methods to screen for ovarian cancer and myocardial infarction

DEPR:

The monoclonal antibody having a high specificity against human Mn-SOD has no reactivity against human Cu, Zn-superoxide dimutase (hereinafter abbreviated as human Cu, Zn-SOD), a human albumin, human globulins. The monoclonal antibody having such specificity can be obtained, for example, by culturing NI8 cell line (FERM-P No. 1606), PE9 cell line (FERM-P No. 1607), PG 11 cell line (FERM-P No. 1608) which are hybridoma cell lines obtained by cell fusion of lymphocytes obtained from a mouse immunized with human Mn-SOD with myeloma cells.

Term	Documents
(9 NOT 6).USPT,PGPB.	1

25

Documents, starting with Document:

Display Format:

**WEST****Generate Collection****Search Results - Record(s) 1 through 5 of 5 returned.** **1. Document ID: US 6033889 A**

L14: Entry 1 of 5

File: USPT

Mar 7, 2000

US-PAT-NO: 6033889

DOCUMENT-IDENTIFIER: US 6033889 A

TITLE: Gene sequence of *Aquifex pyrophilus* superoxide dismutase and protein expressed in *Escherichia coli*

DATE-ISSUED: March 7, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Han; Ye Sun	Seoul			KRX
Yu; Yeon Gyu	Seoul			KRX
Kim; Sung Hou	Berkeley	CA		
Lim; Jae Hwan	Kwachun			KRX
Ryu; Jae Ryeon	Seoul			KRX
Choi; In Geol	Seoul			KRX

US-CL-CURRENT: 435/189; 435/252.8, 435/320.1, 435/325, 435/69.1, 536/23.1,  
536/23.2, 536/24.3, 536/24.32

## ABSTRACT:

Gene sequences of superoxide dismutase of *Aquifex pyrophilus* which is one of hyperthermophile microorganism and protein expressed therefrom are provided, wherein the protein is used as a necessary medicament in treatment of inflammation, disease of autoimmunization, chromosome lesion and the like, and particularly, *A. pyrophilus* is a hyperthermophile which can grow at the optimum temperature of 85.degree. C., and thus the superoxide dismutase of *A. pyrophilus* has a higher thermal stability than other organisms, resulting in further broad applications in the pharmaceutical field.

9 Claims, 9 Drawing figures Exemplary Claim Number: 1  
Number of Drawing Sheets: 9

L14: Entry 1 of 5

File: USPT

Mar 7, 2000

DOCUMENT-IDENTIFIER: US 6033889 A

TITLE: Gene sequence of *Aquifex pyrophilus* superoxide dismutase and protein expressed in *Escherichia coli*

BSPR:

Superoxide dismutase (hereinafter referred to SOD) is an enzyme which can convert superoxide radicals ( $O_{2\cdot}^-$ ) to  $H_2O_2$ . The superoxide radicals are chemically and inevitably generated in vivo. The enzyme is one of the important enzymes to function in the intracellular protection mechanisms. [See, Fridovich, I. et al., Annu. Rev. Biochem. 64, 97-112]. SODs are divided into three species, i.e., Cu- and Zn-, Fe-, and Mn-SOD in accord with the kind of bound metal. Cu-, and Zn-SOD are found in eucaryote, Fe-SOD in eubacteria and archaeobacteria, and Mn-SOD in bacteria and mitochondria of eucaryote.

Full | Title | Citation | Front | Review | Classification | Date | Reference |

KUMC | Draw Desc | Image |

---

2. Document ID: US 5641754 A

L14: Entry 2 of 5

File: USPT

Jun 24, 1997

US-PAT-NO: 5641754

DOCUMENT-IDENTIFIER: US 5641754 A

TITLE: Antisense oligonucleotide compositions for selectively killing cancer cells

DATE-ISSUED: June 24, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Iversen; Patrick L.	Omaha	NE		

US-CL-CURRENT: 514/44; 435/375, 435/6, 435/91.1, 536/23.1, 536/24.5

ABSTRACT:

The present invention relates to methods and compositions for the treatment of cancer using an oligonucleotide and an hydroxyl radical up-regulator. The oligonucleotide is characterized by its ability to down-regulate the path by which the cell repairs oxidative damage to its DNA. Thus, the oligonucleotide renders the tumor cells more susceptible to eradication upon exposure to the hydroxyl radical up-regulator administered substantially concomitantly with or subsequent to administration of the oligonucleotide. This novel treatment, preferentially inhibits the proliferation or kills malignant cells but not normal cells. Preferably, the oligonucleotide is antisense to the gene which encodes protein p53, although other antisense oligonucleotides can also be used. The invention also includes novel conjugates of the oligonucleotide and the hydroxyl up-regulator, as well as new oligonucleotides.

11 Claims, 6 Drawing figures Exemplary Claim Number: 1  
Number of Drawing Sheets: 3

L14: Entry 2 of 5

File: USPT

Jun 24, 1997

DOCUMENT-IDENTIFIER: US 5641754 A

TITLE: Antisense oligonucleotide compositions for selectively killing cancer cells

BSPR:

Most cells normally contain one or more enzyme systems which very rapidly combine with and inactivate excess reactive oxygen species. One of the major enzyme systems in this regard is the superoxide dismutase (SOD) family of metalloenzymes. Superoxide dismutase detoxifies two molecules of superoxide simultaneously, oxidizing one molecule while reducing the other: ##STR1## One form of this metalloenzyme is found in the cytoplasm of eukaryotic cells and contains copper and zinc; a different form is found both in mitochondria and in bacterial cells, and contains manganese; and another related iron-containing form is found in some bacteria, cyanobacteria, and some plants (see, for example, C. K. Matthews and K. E. van Holde, Biochemistry, The Benjamin/Cummings Publishing Company, Inc., Redwood City, Calif., 1990). The wide occurrence of SOD enzymes is confirmation of the biological necessity of rapid inactivation of reactive oxygen intermediates.

Full | Title | Citation | Front | Review | Classification | Date | Reference |

| KWIC | Drawn Desc | Image |

---

3. Document ID: US 4129644 A

L14: Entry 3 of 5

File: USPT

Dec 12, 1978

US-PAT-NO: 4129644

DOCUMENT-IDENTIFIER: US 4129644 A

TITLE: Protecting skin and hair with cosmetic compositions containing superoxide dismutase

DATE-ISSUED: December 12, 1978

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kalopissis; Gregoire	Neuilly-sur-Seine			FRX
Jacquet; Bernard	Antony			FRX
Lang; Gerard	Deuil-la-Barre			FRX

US-CL-CURRENT: 424/59; 424/70.9, 424/74, 424/94.4, 514/773

ABSTRACT:

A hygienic or cosmetic composition for the hair or skin comprises in a cosmetic vehicle at least one superoxide dismutase.

8 Claims, 0 Drawing figures Exemplary Claim Number: 7

L14: Entry 3 of 5

File: USPT

Dec 12, 1978

DOCUMENT-IDENTIFIER: US 4129644 A

TITLE: Protecting skin and hair with cosmetic compositions containing superoxide dismutase

BSPR:

The superoxide dismutases obtained from different marine bacterial strains by the process described above are all superoxide dismutases which include non-hematinic iron, whereas the enzymes exhibiting an activity of superoxide dismutases which are described in the literature mentioned above, i.e. erythrocuprein and an enzyme extract of Escherichia coli, include divalent cations which are, respectively, copper and zinc for the former and manganese for the latter.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KIFC](#) | [Drawn Desc](#) | [Image](#)

---

4. Document ID: US 4029819 A

L14: Entry 4 of 5

File: USPT

Jun 14, 1977

US-PAT-NO: 4029819

DOCUMENT-IDENTIFIER: US 4029819 A

TITLE: Superoxide dismutase and its application as an oxidation inhibitor

DATE-ISSUED: June 14, 1977

INVENTOR-INFORMATION:

NAME	CITY	STATE ZIP CODE	COUNTRY
Michelson; Adolf Michael	Chatenay-Malabry		FR

US-CL-CURRENT: 426/61; 426/7, 435/189

ABSTRACT:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 .+- . 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

6 Claims, 0 Drawing figures Exemplary Claim Number: 1,3

L14: Entry 4 of 5

File: USPT

Jun 14, 1977

DOCUMENT-IDENTIFIER: US 4029819 A

TITLE: Superoxide dismutase and its application as an oxidation inhibitor

ABPL:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 .+- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

BSPR:

The superoxide dismutases obtained from various marine bacterial strains by the process of the invention are all superoxide dismutases comprising non-hematinic iron, while the enzymes having a superoxide dismutase activity which have been previously described and which are erythrocupreine and the enzyme extracted from Escherichia coli comprise divalent cations which are, respectively, copper and zinc for the first and manganese for the second.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KuJC](#) | [Draw. Desc](#) | [Image](#)

---

5. Document ID: US 3997402 A

L14: Entry 5 of 5

File: USPT

Dec 14, 1976

US-PAT-NO: 3997402

DOCUMENT-IDENTIFIER: US 3997402 A

TITLE: Superoxide dismutase and process for production

DATE-ISSUED: December 14, 1976

INVENTOR-INFORMATION:

NAME	CITY	STATE ZIP CODE	COUNTRY
Michelson; Adolf Michael	Chatenay-Malabry		FR

US-CL-CURRENT: 435/189; 435/815, 435/822

ABSTRACT:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 .+- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

14 Claims, 0 Drawing figures Exemplary Claim Number: 10,14

L14: Entry 5 of 5

File: USPT

Dec 14, 1976

DOCUMENT-IDENTIFIER: US 3997402 A

TITLE: Superoxide dismutase and process for production

ABPL:

The invention relates to a process for the production of superoxide dismutase and the superoxide dismutase so obtained. The superoxide dismutase obtained is extracted from marine bacterial strains and is characterized in that it comprises non-hematinic iron or copper and zinc, it has a molecular weight of about 33,000 to 40,000 .+- 2500 and a pH or isoelectric point of about 4 to 8.2 and it has maximum enzyme activity at a pH of about 8.5 to 10 with an optimum at about 9 to 9.5 and the use of said superoxide dismutases for the protection of oxidizable systems from auto-oxidation.

BSPR:

The superoxide dismutases obtained from various marine bacterial strains by the process of the invention are all superoxide dismutases comprising non-hematinic iron, while the enzymes having a superoxide dismutase activity which have been previously described and which are erythrocupreine and the enzyme extracted from Escherichia coli comprise divalent cations which are, respectively, copper and zinc for the first and manganese for the second.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMC](#) | [Draw Desc](#) | [Image](#)

[Generate Collection](#)

Term	Documents
(12 NOT 13).USPT,PGPB.	5

[Display](#)

25

Documents, starting with Document:

5

Display Format:

[REV, K](#)

[Change Format](#)

**WEST****Generate Collection****Search Results - Record(s) 1 through 2 of 2 returned.** **1. Document ID: US 6034219 A**

L18: Entry 1 of 2

File: USPT

Mar 7, 2000

US-PAT-NO: 6034219

DOCUMENT-IDENTIFIER: US 6034219 A

TITLE: Human macrophage antigen

DATE-ISSUED: March 7, 2000

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hillman; Jennifer L.	San Jose	CA		
Au-Young; Janice	Berkeley	CA		
Goli; Surya K.	Sunnyvale	CA		

US-CL-CURRENT: 530/350; 530/387.1, 530/387.9

## ABSTRACT:

The present invention provides a polynucleotide which identifies and encodes a novel human macrophage antigen (TMAH). The invention provides for genetically engineered expression vectors and host cells comprising the nucleic acid sequence encoding TMAH. The invention also provides for the use of substantially purified TMAH and its agonists, antibodies, antagonists or inhibitors in pharmaceutical compositions for treatment of diseases associated with expression of TMAH. The invention also describes diagnostic assays which utilize the polynucleotide to hybridize with the genomic sequence or transcripts encoding TMAH and anti-TMAH antibodies which specifically bind to TMAH.

5 Claims, 5 Drawing figures Exemplary Claim Number: 1  
Number of Drawing Sheets: 8

L18: Entry 1 of 2

File: USPT

Mar 7, 2000

DOCUMENT-IDENTIFIER: US 6034219 A  
TITLE: Human macrophage antigen

## DEPR:

For the production of antibodies, various hosts including goats, rabbits, rats, mice, etc may be immunized by injection with TMAH or any portion, fragment or oligopeptide which retains immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include but are not limited to Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronics polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, and dinitrophenol. BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are potentially useful human adjuvants.

## DEPR:

TMAH substantially purified using PAGE electrophoresis (Sambrook, *supra*) is used to immunize rabbits and to produce antibodies using standard protocols. The amino acid sequence translated from TMAH is analyzed using DNASTar software (DNASTar Inc) to determine regions of high immunogenicity and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Analysis to select appropriate epitopes, such as those near the C-terminus or in hydrophilic regions (shown in FIGS. 4 and 5) is described by Ausubel F M et al (*supra*).

## DEPR:

Typically, the oligopeptides are 15 residues in length, synthesized using an Applied Biosystems Peptide Synthesizer Model 431A using fmoc-chemistry, and coupled to keyhole limpet hemocyanin (KLH, Sigma) by reaction with M-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS; Ausubel F M et al, *supra*). Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. The resulting antisera are tested for antipeptide activity, for example, by binding the peptide to plastic, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radioiodinated, goat anti-rabbit IgG.

## ORPL:

Kroll, J.S., et al., "Copper-Zinc Superoxide Dismutase of *Haemophilus influenzae* and *H. Parainfluenzae*" *J. Bacter.*, 173:7449-7457 (1991).

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KJWC](#) | [Draw Desc](#) | [Image](#)

---

2. Document ID: US 5792648 A

L18: Entry 2 of 2

File: USPT

Aug 11, 1998

US-PAT-NO: 5792648

DOCUMENT-IDENTIFIER: US 5792648 A

TITLE: Human macrophage antigen

DATE-ISSUED: August 11, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Hillman; Jennifer L.	San Jose	CA		
Au-Young; Janice	Berkeley	CA		
Goli; Surya K.	Sunnyvale	CA		

US-CL-CURRENT: 435/252.3; 435/320.1, 435/325, 435/69.1, 536/23.5

ABSTRACT:

The present invention provides a polynucleotide which identifies and encodes a novel human macrophage antigen (TMAH). The invention provides for genetically engineered expression vectors and host cells comprising the nucleic acid sequence encoding TMAH. The invention also provides for the use of substantially purified TMAH and its agonists, antibodies, antagonists or inhibitors in pharmaceutical compositions for treatment of diseases associated with expression of TMAH. The invention also describes diagnostic assays which utilize the polynucleotide to hybridize with the genomic sequence or transcripts encoding TMAH and anti-TMAH antibodies which specifically bind to TMAH.

7 Claims, 8 Drawing figures Exemplary Claim Number: 1

Number of Drawing Sheets: 8

L18: Entry 2 of 2

File: USPT

Aug 11, 1998

DOCUMENT-IDENTIFIER: US 5792648 A

TITLE: Human macrophage antigen

DEPR:

For the production of antibodies, various hosts including goats, rabbits, rats, mice, etc may be immunized by injection with TMAH or any portion, fragment or oligopeptide which retains immunogenic properties. Depending on the host species, various adjuvants may be used to increase immunological response. Such adjuvants include but are not limited to Freund's, mineral gels such as aluminum hydroxide, and surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanin, and dinitrophenol. BCG (bacilli Calmette-Guerin) and Corynebacterium parvum are potentially useful human adjuvants.

DEPR:

TMAH substantially purified using PAGE electrophoresis (Sambrook, *supra*) is used to immunize rabbits and to produce antibodies using standard protocols. The amino acid sequence translated from TMAH is analyzed using DNASTar software (DNASTar Inc) to determine regions of high immunogenicity and a corresponding oligopeptide is synthesized and used to raise antibodies by means known to those of skill in the art. Analysis to select appropriate epitopes, such as those near the C-terminus or in hydrophilic regions (shown in FIGS. 4 and 5) is described by Ausubel F. M. et al (*supra*).

DEPR:

Typically, the oligopeptides are 15 residues in length, synthesized using an Applied Biosystems Peptide Synthesizer Model 431A using fmoc-chemistry, and coupled to keyhole limpet hemocyanin (KLH, Sigma) by reaction with M-maleimidobenzoyl-N-hydroxysuccinimide ester (MBS; Ausubel F. M. et al, *supra*). Rabbits are immunized with the oligopeptide-KLH complex in complete Freund's adjuvant. The resulting antisera are tested for antipeptide activity, for

example, by binding the peptide to plastic, blocking with 1% BSA, reacting with rabbit antisera, washing, and reacting with radioiodinated, goat anti-rabbit IgG.

ORPL:

Kroll, J.S., et al., "Copper-Zinc Superoxide Dismutase of *Haemophilus influenzae* and *H. Parainfluenzae*" *J. Bacter.*, 173:7449-7457 (1991).

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMC](#) | [Draw Desc](#) | [Image](#)

[Generate Collection](#)

Term	Documents
LL5.USPT,PGPB.	70
LL5S	0
(17 AND (LL5 OR 8)).USPT,PGPB.	2

[Display](#)

25

Documents, starting with Document:

2

**Display Format:** [REV, K](#) [Change Format](#)

**WEST****Generate Collection****Search Results - Record(s) 1 through 5 of 5 returned.** **1. Document ID: US 5837500 A**

L23: Entry 1 of 5

File: USPT

Nov 17, 1998

US-PAT-NO: 5837500

DOCUMENT-IDENTIFIER: US 5837500 A

TITLE: Directed evolution of novel binding proteins

DATE-ISSUED: November 17, 1998

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert Charles	Ijamsville	MD		
Gutterman; Sonia Kosow	Belmont	MA		
Roberts; Bruce Lindsay	Milford	MA		
Markland; William	Milford	MA		
Ley; Arthur Charles	Newton	MA		
Kent; Rachel Baribault	Boxborough	MA		

US-CL-CURRENT: 435/69.7; 435/471, 435/91.1, 435/91.2, 530/350, 530/412, 536/23.4

## ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

43 Claims, 16 Drawing figures Exemplary Claim Number: 1  
Number of Drawing Sheets: 16

L23: Entry 1 of 5

File: USPT

Nov 17, 1998

DOCUMENT-IDENTIFIER: US 5837500 A  
TITLE: Directed evolution of novel binding proteins

## DEPL:

Dougan, G, and P Morrissey, "Molecular analysis of the virulence determinants of enterotoxigenic Escherichia coli isolated from domestic animals: applications for vaccine development", Vet Microbiol (1984/5), 10: 241-57.

## DETL:

1) (CYS).sub.4 :Fe Rubredoxin (in CREI84, P.376) 2) (CYS).sub.4 :Zn Aspartate Transcarbamylase (in CREI84, P.376) and Zn-fingers (HARD90) 3) (HIS).sub.2 (MET)(CYS):Cu Azurin (in CREI84, P.376) and Basic "Blue" Cu Cucumber protein (GUSS88) 4) (HIS).sub.4 :Cu CuZn superoxide dismutase 5) (CYS).sub.4 :(Fe.sub.4 S.sub.4) Ferredoxin (in CREI84, P.376) 6) (CYS).sub.2 (HIS).sub.2 :Zn Zinc-fingers (GIBS88) 7) (CYS).sub.3 (HIS):Zn Zinc-fingers (GAUS87, GIBS88)

## ORPL:

Clements, John D. "Construction of a nontoxic fusion peptide for immunization against escherichia coli strains that produce heat-labile and heat-stable enterotoxins", Infection and Immunity (1990), 58(5):1159-66.

## ORPL:

Dougan, G, and P Morrissey, "Molecular analysis of the virulence determinants of enterotoxigenic Escherichia coli isolated from domestic animals: applications for vaccine development", Vet Microbiol (1984/5), 10:241-57.

## ORPL:

Houghten, et al. "A completely synthetic toxoid vaccine containing Escherichia coli heat-stable toxin and antigenic determinants of the heat-liabile toxin B subunit", Infection and Immunity (1985), 48(3):735-740.

## ORPL:

Wu, et al. "Expression of immunogenic epitopes of hepatitis B surface antigen with hybrid flagellin proteins by a vaccine strain of Salmonella", PNAS (1989), 86:4726-30.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KDDC](#) | [Draw Desc](#) | [Image](#)

---

2. Document ID: US 5571698 A

L23: Entry 2 of 5

File: USPT

Nov 5, 1996

US-PAT-NO: 5571698

DOCUMENT-IDENTIFIER: US 5571698 A

TITLE: Directed evolution of novel binding proteins

DATE-ISSUED: November 5, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert C.	Ijamsville	MD		
Guterman; Sonia K.	Belmont	MA		
Roberts; Bruce L.	Milford	MA		
Markland; William	Milford	MA		
Ley; Arthur C.	Newton	MA		
Kent; Rachel B.	Boxborough	MA		

US-CL-CURRENT: 435/69.7; 435/252.3, 435/320.1, 435/477, 435/6, 435/59.1

ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

83 Claims, 16 Drawing figures Exemplary Claim Number: 1

Number of Drawing Sheets: 16

L23: Entry 2 of 5

File: USPT

Nov 5, 1996

DOCUMENT-IDENTIFIER: US 5571698 A

TITLE: Directed evolution of novel binding proteins

DEPR:

DOUG84: Dougan, G, and P Morrissey, "Molecular analysis of the virulence determinants of enterotoxigenic Escherichia coli isolated from domestic animals: applications for vaccine development", Vet Microbiol (1984/5), 10:241-57.

DETL:

1) (CYS).sub.4 :Fe Rubredoxin (in CREI84, P. 376) 2) (CYS).sub.4 :Zn Aspartate Transcarbamylase (in CREI84, P. 376) and Zn-fingers (HARD90) 3) (HIS).sub.2 (MET)(CYS):Cu Azurin (in CREI84, P. 376) and Basic "Blue" Cu Cucumber protein (GUSS88) 4) (HIS).sub.4 :Cu CuZn superoxide dismutase 5) (CYS).sub.4 :(Fe.sub.4 S.sub.4) Ferredoxin (in CREI84, P. 376) 6) (CYS).sub.2 (HIS).sub.2 :Zn Zinc-fingers (GIBS88) 7) (CYS).sub.3 (HIS):Zn Zinc-fingers (GAUS87, GIBS88)

3. Document ID: US 5403484 A

L23: Entry 3 of 5

File: USPT

Apr 4, 1995

US-PAT-NO: 5403484

DOCUMENT-IDENTIFIER: US 5403484 A

TITLE: Viruses expressing chimeric binding proteins

DATE-ISSUED: April 4, 1995

## INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert C.	Ijamsville	MD		
Guterman; Sonia K.	Belmont	MA		
Roberts; Bruce L.	Milford	MA		
Markland; William	Milford	MA		
Ley; Arthur C.	Newton	MA		
Kent; Rachel B.	Boxborough	MA		

US-CL-CURRENT: 435/235.1; 435/252.3, 435/320.1, 435/69.7, 530/350, 536/23.4

## ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

49 Claims, 16 Drawing figures Exemplary Claim Number: 1

Number of Drawing Sheets: 16

L23: Entry 3 of 5

File: USPT

Apr 4, 1995

DOCUMENT-IDENTIFIER: US 5403484 A  
TITLE: Viruses expressing chimeric binding proteins

## DETL:

1) (CYS).sub.4 :Fe Rubredoxin (in CREI84, P. 376) 2) (CYS).sub.4 :Zn Aspartate Transcarbamylase (in CREI84, P. 376) and Zn-fingers (HARD90) 3) (HIS).sub.2 (MET)(CYS):Cu Azurin (in CREI84, P. 376) and Basic "Blue" Cu Cucumber protein (GUSS88) 4) (HIS).sub.4 :Cu CuZn superoxide dismutase 5) (CYS).sub.4 :(Fe.sub.4 S.sub.4) Ferredoxin (in CREI84, P. 376) 6) (CYS).sub.2 (HIS).sub.2 :Zn Zinc-fingers (GIBS88) 7) (CYS).sub.3 (HIS):Zn Zinc-fingers (GAUS87, GIBS88)

## ORPL:

CLEM90 Clements, John D. "Construction of a nontoxic fusion peptide for immunization against Escherichia coli strains that produce heat-labile and heat-stable enterotoxins" Infection and Immunity (1990), 58(5):1159-66.

## ORPL:

DOUG84: Dougan, G, and P Morrissey, "Molecular analysis of the virulence determinants of enterotoxigenic Escherichia coli isolated from domestic animals: applications for vaccine development", Vet Microbiol (1984/5), 10:241-57.

## ORPL:

HOUG85: Houghten, et al. "A completely synthetic toxoid vaccine containing Escherichia coli heat-stable toxin and antigenic determinants of the heat-labile toxin B subunit", Infection and Immunity (1985), 48(3):735-740.

## ORPL:

WUJY89: Wu, et al. "Expression of immunogenic epitopes of hepatitis B surface antigen with hybrid flagellin proteins by a vaccine strain of Salmonella", PNAS (1989), 86:4726-30.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [KMC](#) | [Draw Desc](#) | [Image](#)

---

4. Document ID: US 5366729 A

L23: Entry 4 of 5

File: USPT

Nov 22, 1994

US-PAT-NO: 5366729

DOCUMENT-IDENTIFIER: US 5366729 A

TITLE: Non-glycosylated variants of extracellular superoxide dismutase (EC-SOD)

DATE-ISSUED: November 22, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Marklund; Stefan	Ume.ang.			SEX
Edlund; Thomas	Ume.ang.			SEX

US-CL-CURRENT: 424/94.4; 435/189, 435/320.1, 435/325, 435/358, 536/23.2

ABSTRACT:

Extracellular superoxide dismutase (EC-SOD) variants having the superoxide dismutating property of the native EC-SOD and having a modified (reduced or increased) binding to heparin as compared to recombinant EC-SOD C as well as compositions comprising such variants. The EC-SOD variants are polypeptides comprising: 1) amino acids 1-193 of native EC-SOD C and 2) an amino acid sequence which is based on, but different from amino acid moieties 194-222 of recombinant EC-SOD C, either by being truncated or prolonged at the C-terminal end or by having substituted or otherwise modified one or more amino acid moieties of the sequence. Another EC-SOD variant is one which differs from recombinant EC-SOD C by being a glycosylation-free mutant. The variants may be produced by recombinant DNA techniques and are useful in the treatment of various diseases.

14 Claims, 20 Drawing figures Exemplary Claim Number: 1

Number of Drawing Sheets: 27

L23: Entry 4 of 5

File: USPT

Nov 22, 1994

DOCUMENT-IDENTIFIER: US 5366729 A

TITLE: Non-glycosylated variants of extracellular superoxide dismutase (EC-SOD)

BSPR:

Organisms living in the presence of oxygen have been forced to develop a number of protective mechanisms against toxic oxygen reduction metabolites, such as superoxide radicals, which are formed in connection with a variety of biological oxidations. The protective factors include superoxide dismutases (SOD) (superoxide:superoxide oxidoreductase, EC 1.15.1.1) which dismutate the superoxide radical and are found in relatively constant amounts in mammalian cells and tissue. The best known of these enzymes is CuZn SOD which is a dimer with a molecular weight of 33,000 containing two copper and two zinc atoms. CuZn SOD is found in the cytosol and in the intermembrane space of the mitochondria. Mn SOD is a tetramer with a molecular weight of 85,000 containing 4 Mn atoms, and is mainly located in the mitochondrial matrix. Recently, a superoxide dismutase was found in the extracellular fluids of mammals, birds and fish. This superoxide dismutase has been denoted extracellular superoxide dismutase which in the following will be termed EC-SOD.

BSPR:

EC-SOD is a tetrameric Cu and Zn containing glycoprotein (S. L. Marklund, Proc. Natl. Acad. Sci. USA. 79, 1982, pp. 7634-7638; L. Tibell et al., Proc. Natl. Acad. Sci. USA. 84, 1987, pp. 6634-6638). A cDNA sequence encoding EC-SOD has been elucidated and useful applications of the cDNA and the EC-SOD encoded thereby are described in WO 87/01387, the contents of which are hereby incorporated by reference. The cDNA sequence is the sequence shown in FIG. 1A and FIG. 1B corresponding to amino acid residues 1-222 (without any mutations). EC-SOD is a secretory protein and the cDNA encodes an 18 amino acids long signal sequence which is absent in mature and recombinant EC-SOD (L. Tibell et al., Proc. Natl. Acad. Sci. USA. 84, 1987, pp. 6634-6638). As deduced from the cDNA

sequence, the subunit molecular weight of the mature enzyme is 24,200. The exact size of the carbohydrate substituent is not known, but the apparent molecular weight on gel chromatography of the tetramer is 140-150 kDa. On SDS-PAGE electrophoresis the subunits display a molecular weight of 30-32 kDa (L. Tibell et al., Proc. Natl. Acad. Sci. USA. 84, 1987, pp. 6634-6638). The sequence contains one glycosylation site Asn-89 (K. Hjalmarsson et al., Proc. Natl. Acad. Sci. USA. 84, 1987, pp. 6340-6344), and the mature enzyme binds to the lectins concanavalin A, wheat germ lectin and lentil lectin. The tetramers contain 4 Cu and 4 Zn atoms. The active site, which contains the metal atoms, is homologous to the active site of the intracellular CuZn SODs (K. Hjalmarsson et al., Proc. Natl. Acad. Sci. USA. 84, 1987, pp. 6340-6344).

BSPR:

The formula A-R outlined above of the polypeptide of the invention is constituted of two parts; the first part is the amino acid sequence of EC-SOD C from and including amino acid 1 and up to and including amino acid 193. The entire EC-SOD sequence is constituted of 222 amino acids, not all of which are required for conferring the superoxide dismutating property to native EC-SOD C. Thus, by comparison of the amino acid sequence with Cu Zn SODs of various origins, a possible active site of the enzyme has been found between amino acid 97 and amino acid 193 of the amino acid sequence encoding EC-SOD C. This part of EC-SOD C is believed to be essential for the superoxide dismutating property of the enzyme. The part of the EC-SOD C constituting amino acid 1-96 is contemplated to be involved in the formation of oligomers of the polypeptide. However, in accordance with what is stated above, modifications within the part of the EC-SOD C sequence constituting amino acids 1-193, which modifications do not impair the superoxide dismutating property of the enzyme should be considered as modifications of the polypeptide of the invention in accordance with the definition given above. Based on the above-mentioned homology between the active sites of the various SOD enzymes, modifications in the part of the EC-SOD C sequence constituting amino acids 1-193 could be performed by site-directed mutagenesis so that the active site of the enzyme remains active. How to perform such modifications is explained in further details below. The amino acid sequence R of the polypeptide of the invention is the part of the polypeptide which has been found, according to the invention, to be relevant with respect to modifications of the heparin affinity of the enzyme. Normally, R is based on the amino acids moieties 194-222 of recombinant EC-SOD C, i.e. the amino acid moieties of the C-terminal part of EC-SOD C, R, however, having been changed in accordance with the present invention in such a manner that a reduced or an increased affinity for heparin has been obtained compared to the heparin affinity of recombinant EC-SOD C. The changes of the C-terminal part of EC-SOD C which produce the amino acid sequence R will be further dealt with in the following. In addition to such changes, R may in some cases have been subjected to modifications as defined above, e.g. modifications in R which are not involved in the heparin binding.

BSPR:

The medium used to grow the cells may be any conventional medium suitable for the purpose. Because of the high degree of similarity of the polypeptide of the invention and EC-SOD, the polypeptide of the invention is believed to contain Cu and Zn and it may be necessary to add extra Cu and/or Zn for the synthesis of the polypeptide of the invention, especially if the polypeptide is to be produced in increased amounts. A suitable vector may be any of the vectors described above, and an appropriate host cell may be any of the cell types listed above. The methods employed to construct the vector and effect introduction thereof into the host cell may be any methods known for such purposes within the field of recombinant DNA.

BSPR:

When using a monoclonal antibody for the recovering of the polypeptide of the invention, it may be produced by a hybridoma technique which is well-known method for producing antibodies. In the hybridoma technique using, for instance, mice as the animals immunized, mice are immunized with the antigen in question and spleen cells from the immunized mice are fused with myeloma cells whereupon the fused hybridoma cells are cloned, antibody-producing cells are grown in a

suitable growth medium and the antibodies are recovered from the culture. The antibodies obtained by the hybridoma technique have the advantage of greater specificity and, hence, a greater purifying potential as mentioned above. In a possible further step, using recombinant DNA techniques, the DNA sequence encoding the antibody is transferred from the hybridoma cell clone to a suitable vector, the hybrid vector is transformed to a suitable bacterial host, the host is grown in an appropriate medium and the resulting antibody is recovered from the culture. In this way, an improved yield of antibody may be obtained. The host may be one usually employed in the field of recombinant DNA technology such as Escherichia coli or Bacillus subtilis.

BSPR:

Thus, the polypeptide of the invention is indicated for substantially the same applications as CuZn SOD the therapeutic activity of which has been more thoroughly documented as discussed below. EC-SOD and the EC-SOD variants of the invention have, however, been found to possess a number of characteristics which are assumed to make them particularly useful for therapeutic applications. The property of the new EC-SOD variants of the invention of having a heparin affinity different from that of recombinant EC-SOD C is likely to confer upon them a considerable advantage in terms of therapeutic usefulness, as compared with recombinant EC-SOD C.

BSPR:

CuZn SOD has a low molecular weight (33,000) which causes it to become eliminated very quickly by glomerular filtration in the kidneys so that in rodents it has a plasma half-life of less than 10 minutes and, in human beings, the enzyme has a half-life of about 20-30 minutes. EC-SOD C (K. Karlsson et al., J. Clin. Invest. 82, 1988, pp. 762-766) and the EC-SOD variants presented in this application (Examples 1, 2, & 4) have a much longer half-life. This is partly due to the high molecular weight of EC-SOD and EC-SOD variants of the invention which prevents them from being eliminated by glomerular filtration, and partly due to the fact that EC-SOD and EC-SOD variants of the invention of the C-type seem to bind to endothelial cell surfaces (K. Karlsson et al., Biochem. J. 242, 1987, pp. 55-59; K. Karlsson et al., Biochem. J. 255, 1988, pp. 223-228; K. Karlsson et al., J. Clin. Invest. 82, 1988, pp. 762-766; K. Karlsson et al., Lab. Invest. 60, 1989, pp. 659-666). In the therapeutic use of EC-SOD and variants according to the invention, the enzyme therefore preferably has a half-life in human beings of at least 4 hours and possibly even longer.

BSPR:

The significance of the apparent association of EC-SOD and EC-SOD variants of the invention with cell membranes is further supported the finding that CuZn SOD which has been modified with polylysine to bind to cell membranes is better able to protect activated (superoxide radical-producing) polymorphonuclear leukocytes (PMN) from autoinactivation (cell death) than normal CuZn SOD which is negatively charged and therefore tends to be repelled by the cell membranes (M. Salin and J. M. Mc Cord, "Free radicals in leukocyte metabolism and inflammation", in Superoxide and Superoxide Dismutases, eds. A. M. Michelson, J. M. McCord and I. Fridovich, Academic Press, 1977, pp. 257-270). The fact that Nocardia asteroides possesses a membrane-associated SOD which appears to confer efficient protection against activated human PMNs as the susceptibility of Nocardia to PMNs is significantly increased when Nocardia cells are treated with antibodies towards this SOD (B. L. Beaman et al., Infect. Immun. 47, 1985, pp. 135-141) also points to a cell membrane-protective function of SOD bound to cell surfaces. Unlike EC-SOD and EC-SOD variants or the invention, CuZn SOD has an intracellular function which may make it less well suited for extracellular application, i.e. occasioned by the extracellular presence of superoxide radicals. Furthermore, its brief half-life compared to that of EC-SOD and EC-SOD variants or the invention mentioned above would seem to make it necessary to administer larger doses at shorter intervals than is likely to be the case with the EC-SOD variants of the invention.

BSPR:

Parenterally administered CuZn SOD has been shown to exhibit an anti-inflammatory effect in a series of animal models of inflammation as well as

in inflammatory diseases in animals (Huber and Saifer, in Superoxide and Superoxide Dismutases, eds. Michelson et al., Academic Press, 1977, pp. 517-549). In humans, positive effects of CuZn SOD has been reported in rheumatoid arthritis and arthroses, in inflammation of the bladder and other urological conditions (Menander-Huber in Biological and Clinical Aspects of Superoxide and Superoxide Dismutase, eds. Bannister et al., Elsevier/North Holland, 1980, pp. 408-423) as well as adverse effects of treatment with ionizing radiation (Edsmyr et al. Current Therapy. Res. 10, 1976, pp. 198-211; Cividalli et al., Acta Radiol. Oncol. 24, 1985, pp. 273-277 (in rats)). In some countries, bovine CuZn SOD has become registered as a drug (Orgotein, Peroxinorm), employed mainly for the treatment of arthritis and arthroses where the composition is administered intraarticularly (Goebel and Storck, Am. J. Med. 74, 1983, pp. 124-128), but also for urological conditions.

BSPR:

Parenterally administered CuZn SOD is not taken up by the cells and must exert its activity in the extracellular space. CuZn SOD encapsulated in liposomes is taken up by the cells and is reported to be effective against Crohn's disease, Bechet's disease, dermatitis herpetiformis, ulcerative colitis, Kawasaki's disease and against the adverse effects of radiation therapy (Y. Niwa et al., Free Rad. Res. Comms. 1, 1985, pp. 137-153). The mechanism of the anti-inflammatory activity of CuZn SOD is not quite clear. Direct protection against oxygen radicals formed by activated leukocytes has been suggested (Halliwell, Cell Biol. Int. Rep. 6, 1982, pp. 529-541). Another possibility is prevention of the formation of a superoxide induced strongly chemotaxic substance (Petrone et al., Proc. Natl. Acad. Sci. USA 77, 1980, pp. 1159-1163).

BSPR:

The other large potential area of application for SOD is as a protective factor against tissue damage caused by ischaemia followed by reperfusion. If the supply of blood to a tissue is cut off, the tissue will slowly become necrotic. Macro- and microscopically the damage will typically develop slowly over many hours. If the tissue is reperfused after, for instance, one hour, a strong acceleration of the tissue damage will occur instead of an improvement. Most likely there are several reasons for this so-called reperfusion paradox, but oxygen radicals formed as a result of the reappearance of oxygen in previously ischaemic tissue appear to contribute to the damage. The radicals are extremely shortlived and therefore difficult to study directly, and much of the information concerning their formation and effects is inferred from the protective action of various oxygen radical scavengers. Their formation have however also been demonstrated more directly by means of EPR on heart samples (Zweier et al., J. Clin. Invest. 80, 1987, pp. 1728-1734) and by means of spin traps in heart reperfusion (e.g. P. B. Garlick et al., Circ. Res. 61, 1987, 751-760; R. Bolli et al., J. Clin. Invest. 82, 1988, 476-485). Tissue protection by means of CuZn SOD has been demonstrated in ischaemia- or anoxia-reperfusion models in the kidney (G. L. Baker et al., Am. Surg. 202, 1985, pp. 628-641; I. Koyama et al., Transplantation 40, 1985, pp. 590-595; E. Hansson et al., Clin. Sci. 65, 1983, pp. 605-610; A. Bayati et al., Acta Physiol. Stand. 130, 1987, pp. 367-372; J. F. Bennett et al., Cryobiology 24, 1987, pp. 264-269; T. Hoshino et al., Transplantation 45, 1988, pp. 284-289; P. J. Bosco et al., Arch. Surg. 123, 1988, pp. 601-604), intestine (D. A. Parks et al., Gastroenterology 82, 1982, pp. 9-15; M. H. Schoenberg et al., Acta Chim. Scand. 150, 1984, pp. 301-309; M. C. Dalsing et al., J. Surg. Res. 34, 1983, pp. 589-596; M. Younes et al., Res. Exp. Med. 187, 1987, pp. 9-17), pancreas (H. Sanfey et al., Ann. Surg. 200, 1983, pp. 405-413), liver (S. L. Atalla et al., Transplantation 40, 1985, pp. 584-589; G. Nordstrom et al., Circ. Shock 26, 1988, pp. 115-126), lung (R. S. Stuart et al., Transplant. Proc. 17, 1985, pp. 1454-1456; I. Koyama et al., I. Koyama et al., J. Appl. Physiol., 63, 1987, pp. 111-115), skeletal muscle (R. V. Korthuis, Circ. Res. 57, 1985, pp. 599-609), skin (M. J. Im et al., Ann. Surg. 201, 1985, pp. 357-359; A. Sagi et al., Plast. Reconstr. Surg. 77, 1986, pp. 639-642; L. Huang et al., FASEB J. 1, 1987, pp. 129-132; T. J. Zimmerman et al., Ann. Plast. Surg. 18, 1987, pp. 218-223; A. T. Pokorny et al., Arch. Otolaryngol. Head Neck Surg. 115, 1989, pp. 207-212), brain (J. P. Pigott et al., J. Vasc. Surg. 7, 1988, pp. 625-630; T. H. Liu et al., Am. J. Physiol. 256, 1989, pp. H589-H593), spinal cord (K. H. Lim et al., Ann. Thorac. Surg. 42, 1986, pp.

282-286; P. Cuevas et al., Anat. Embryol. 179, 1989, 251-255), and bone tissue (A.-P. C. Weiss et al., Plast. Reconstr. Surg. 82, 1988, pp. 486-495).

BSPR:

Preservation of heart function has been reported in isolated, perfused preparations from the cat (M. Schlafer et al., Circulation 66, Suppl. I, 1982, pp. 185-192) and rat (Gaudel et al., J. Mol. Cell Cardiol. 16, 1984, pp. 459-470). In regional ischaemia-reperfusion models in vivo, reduction of infarct size has been reported in the dog (T. J. Gardner et al., Surgery 94, 1983, pp. 423-427; D. E. Chambers et al., J. Mol. Cell Cardiol. 17, 1985, pp. 145-152; S. W. Werns et al., Circ. Res. 56, 1985, pp. 895-898; G. Ambrosio et al., Circulation 72, 1986, pp. 1424-1433), in the pig (U. Naslund et al., J. Mol. Cell Cardiol. 18, 1986, pp. 1077-1084) and the rat (N. Aoki et al., Br. J. Pharmacol. 95, 1988, pp. 735-740). Protection by CuZn SOD has also been reported in models designed to mimic heart transplantation (M. J. Jurmann et al., J. Thorac. Cardiovasc. Surg. 95, 1988, pp. 368-377; F. Gharagozloo et al., J. Thorac. Cardiovasc. Surg. 95, 1988, pp. 1008-1013; J. R. Stewart et al., Ann. Thorac. Surg. 42, 1986, pp. 390-393) and reperfusion after cardiopulmonary bypass (F. Gharagozloo et al., J. Thorac. Cardiovasc. Surg. 95, 1988, pp. 631-636). Injection of SOD+catalase has also been reported to preserve the mechanical heart function after a brief (15 minutes) regional ischaemia in the dog (M. L. Myers et al., Circulation 72, 1985, pp. 915-921; K. Przyklenk and R. A. Kloner, Circ. Res. 58 1986, pp. 148-156). Furthermore, SOD has been reported to reduce the incidence of ischaemia-and-reperfusion induced arrhythmias (B. Woodward et al., J. Mol. Cell. Cariol. 17, 1985, pp. 485-493; M. Bernier et al., Circ. Res. 58, 1986, pp. 331-340; Tamwray et al., Circ. Res. 63, 1988, pp. 944-959). It is contemplated that EC-SOD and EC-SOD variants of the invention might be used in connection with thrombolytic agents such as streptokinase, tissue plasminogen activator, urokinase and variants and variants of these factors. Enhanced myocardial salvage by the combined treatment with urokinase and CuZn SOD (U. Fincke et al., Arzneim.-Forsch./Drug Res. 38, 1988, pp. 138-142) has been reported in a canine coronary thrombosis model.

BSPR:

Furthermore CuZn SOD has been shown to enhance the thrombolytic effects of tissue plasminogen activator in the dog heart. The result was hypothesized to be due to preservation of Endothelin-Derived Relaxation Factor (EDRF), resulting in reduced platelet aggregation and better vasodilation during reperfusion (J. L. Mehta et al., Doctoral thesis, Faculty of Medicine, Upsaliensis, no. 215, 1989, Acta Universitatis).

BSPR:

A variety of gastroenterological application are suggested by results in the literature. Parenteral CuZn SOD ameliorates experimental necrotizing enterocolitis in rabbits (D. A. Clark et al., Am. J. Path. 130, 1988, pp. 537-542; M. J. S. Miller et al., Am. J. Physiol. 255, 1988, pp. G556-G565). A protection of gastric mucosa by parenteral CuZn SOD against the effects of a variety of agents has been reported in animal models; temporary reduction of celiac artery pressure (M. A. Perry et al., Gastroenterology 90, 1986, pp. 362-367), haemorrhagic shock (C. von Ritter et al., Dig. Dis. Sci. 33, 1988, pp. 857864; M. Itoh et al., Gastroenterology 88, 1985, 1162-1167), ethanol and aspirin administration (G. Pihan et al., Digest. Dis. Sci. 32, 1987, pp. 1395-1401), and *E. coli* sepsis (S. Arvidsson et al., Circ. Shock 16, 1985, pp. 383-393). The wound margin strength after intestinal anastomosis is enhanced by parenteral CuZn SOD (H. Hogstrom and U. Haglund, Surgery 99, 1986, 716-720).

BSPR:

Hepatitis and hepatic injury experimentally induced by many means is counteracted by parenteral CuZn SOD; ethanol (M. Younes et al., Free Rad. Res. Comms. 3, 1987, pp. 19-26); *corynebacterium parvum* plus endotoxin (M. J. P. Arthur et al., Gastroenterology 89, 1985, pp. 1114-1122); injection of galactoseamine and galactoseamine-latex particles (Y. Shiratori et al., Hepatology 8, 1988, pp. 815-821); injection of galactoseamine plus endotoxin (A. Wendel et al., Biochem. Pharmacol. 36, 1987, pp. 2637-2639); and hypoxia (A. Yoshioka et al., J. Dermatol. 14, 1987, pp. 569-575).

## BSPR:

Parenterally administered CuZn SOD also ameliorates acute pancreatitis induced by infusion of oleic acid, partial obstruction of the excretory ducts and ischaemia followed by reperfusion (Sanfrey et al., Ann. Surg. 200, 1984, pp. 405-413); and by cerulein-infusion (K. S. Gulce et al., Am. J. Surg. 151, 1986, pp. 163-169; A. Dabrowski et al., Scand. J. Gastroenterol. 23, 1988, pp. 1245-1249; J. Wisher et al., Gut 29, 1988, pp. 1516-1523). The results indicate the possibility of an active therapy against this disease for which no specific therapy exists at present.

## BSPR:

It has also been suggested that treatment with SOD is effective against burns. The local oedema after an experimental slight burn in rats could be somewhat decreased through injection of SOD (Bjork and Artursson, Burns 9, 1983, pp. 249-256). In an animal model involving severe burn damage of mice a dramatic protection was obtained by means of SOD, where survival and local damage were concerned (Saez et al., Circulatory Shock 12, 1984, pp. 220-239). Burn-induced intravascular hemolysis is reduced by polyethyleneglycol- substituted CuZn SOD (Hatherill et al., J. Clin. Invest. 78, pp. 629-636) as is burn-induced myocardial depression (J. W. Horton et al., J. Burn Care Rehabil. 9, 1988, pp. 589-598).

## BSPR:

In the case of, for instance, burns, immunocomplex formation, and major tissue damage, neutrophilic leukocytes are accumulated in the lungs. Complement activation (C5 a) often seems to mediate the accumulation. The leukocytes seem to be activated and release oxygen radicals, thereby causing lung damage which, for instance, is characterized by increased vessel permeability and lung oedema (adult respiratory distress). In several animal models, SOD and other oxygen radical scavengers have been shown to have a protective effect against lung damage (Till and Ward, Agents and Actions, Suppl. 12, 1983, pp. 383-396). Protection by CuZn SOD against other lung damage models have also been reported; oedema formation during perfusion (B. Risberg et al., Eur. Surg. Res. 17, 1985, pp. 230-236); intrabronchial installation of Phorbol Myristate Acetate (PMA) (I. U. Schraufstatter et al., J. Clin. Invest. 73, 1984, pp. 1175-1184; J. S. Kerr et al., Agent. Action. 21, 1987, pp. 293-296); xanthine oxidase (O. D. Saugstad et al., Intensive Care Med. 13, 1987, pp. 30-32); or hyperoxia (R. V. Padmanabhan et al., Am. Rev. Respir. Dis. 132, 1985, pp. 164-167).

## BSPR:

Parenterally administered CuZn SOD has been reported to prevent bronchopulmonary dysplasia in preterm neonates suffering from infantile respiratory distress (W. Rosenfeld et al., J. Pediatr. 105, 1984, pp. 781-785).

## BSPR:

Concerning the central nervous system, protective effects of CuZn SOD have been shown against posttraumatic brain oedema (P. H. Chan et al., Ann. Neurol. 21, 1987, pp. 540-547) and experimental autoimmune neuritis (H.-P. Hartung et al., Ann. Neurol. 23, 1988, pp. 453-460). In a beagle puppy model, injection of SOD has been reported to reduce the frequency of intraventricular brain haemorrhage following hypotension (L. R. Ment et al., J. Neurosurg. 62, 1985, J63-J69).

## BSPR:

CuZn SOD+catalase in the medium have been reported to prolong the survival of the perfused isolated rabbit cornea (O. N. Lux et al., Curr. Eye Res. 4, 1985, pp. 153-154). CuZn SOD+catalase protect the isolated lens against photoperoxidation (S. D. Varma et al., Ophthalmic Res. 14, 1982, pp. 167-175). The results suggest possible beneficial effects of SOD in cornea transplantsations and other ophthalmic surgical procedures. Parenteral CuZn SOD protects against uveitis induced by injection of lens protein (N. A. Rao et al., Ophthalmic Res. 18, 1986, pp. 41-46) and soluble retinal antigen (N. A. Rao et al., Invest. Ophthalmol. Visual Sci. 28, 1987, pp. 886-892).

## BSPR:

In various types of autoimmune disease, such as systemic lupus erythematosus (SLE), systemic sclerosis and rheumatoid arthritis, an increased frequency of chromosomal breaks in lymphocytes has been demonstrated (Emerit, "Properties and action mechanisms of clastogenic factors", in Lymphokines, Vol. 8, ed. E. Pick, Academic Press, 1983, pp. 413-424). Fibroblast cultures and direct bone marrow preparations also sometimes show increased breakage. Plasma from such patients contains a chromosome breaking--clastogenic--factor. In some instances a similar factor has also been demonstrated in synovial fluid and in cerebrospinal fluid (disseminated sclerosis). Breaks occur in normal lymphocytes which are cocultivated with lymphocytes from patients with autoimmune disease. Lymphocytes from patients condition culture media to produce chromosome breaks. The clastogenic activity of SLE plasma can be increased by UV-irradiation. Production of superoxide in plasma by means of xanthine oxidase and xanthine results in formation of clastogenic activity. In all the above described models, addition of CuZn SOD to the medium protected against the clastogenic activity (Emerit, ibid.). This indicates that superoxide radicals are involved in both the formation and actions of the clastogenic factor (Emerit, ibid.). In an animal model of SLE, the New Zealand black mouse which possesses the clastogenic factor, the chromosomes are protected in bone marrow cells in vivo by repeated injections of SOD (Emerit et al., Cytogenet. Cell Genet. 30, 1982, pp. 65-69). It is, however, still unclear to what extent the clastogenic factor contributes to the major symptoms in human autoimmune disease and whether administration of SOD has any therapeutic effect.

**BSPR:**

It has been described (Roberts et al., J. Urol. 128, 1982, pp. 1394-1400; A. Kaur et al., Biochem. Int. 16, 1988, pp. 1083-1094) that parenteral CuZn SOD protects kidneys against experimentally induced pyelonephritis. CuZn SOD protects against acute nephritis induced in rats by anti-glomerular basement membrane antibodies (A. Rehan et al., Lab. Invest. 51, 1984, pp. 396-403), and nephrotoxic serum (T. Adachi et al., Biochem. Pharmacol. 35, 1986, pp. 341-345). Furthermore a protection against aminonucleoside nephritis has been demonstrated (J. R. Diamond et al., Kidney Int. 29, 1986, pp. 478-483; M. Beaman et al., Clin. Sci. 73, 1987, pp. 329-332).

**BSPR:**

Generally, CuZn SOD has been employed as the test substance in the experiments described above. It is, however, assumed that EC-SOD variants of the invention may be employed for the same purposes and, as has been indicated above, with greater efficiency due to its particular properties which may make it especially attractive to employ EC-SOD variants of the invention extracellularly.

**BSPR:**

Recombinant EC-SOD C has been found to be more efficient than CuZn SOD in disease models in which the two SODs have been tested in parallel. Thus, as described by Johansson et al., Cardiovascular Research 24, 1990, pp. 500-503, recombinant EC-SOD C has been shown to reduce the concentration of oxygen-free radicals in reperfused rat hearts. The effect of rEC-SOD C in reducing the free radical concentrations was concluded to be at least of the same extent as CuZn SOD. Furthermore, recombinant human EC-SOD C has been shown to reduce myocardial damage in rats subjected to ischemia and 24 hours of reperfusion (G. Wahlund et al., J. Mol. Cell. Cardiol. 22, Suppl. 1 III, 1990, p. 47). In contrast, CuZn SOD did not show a significant induction of myocardial damage 24 hours after onset of reperfusion. M. Erlansson et al., Free Rad. Biol. Med., in press 1990 discloses the use of EC-SOD C and bovine CuZn SOD as an inhibitor of post-ischemic microvascular permeability increase in hamsters.

**BSPR:**

The estimate of a suitable, i.e. therapeutically active, dosage for systemic treatment is made on the basis of the content of EC-SOD in the human body. EC-SOD is the major SOD in human plasma, and the total activity (composed of fractions A, B, and C; K. Karlsson et al., Biochem. J. 242, 1987, pp. 55-59) is about 20 U/ml. Injection of 200 IU heparin per kg body weight results in an increase of EC-SOD fraction C of about 23 U/ml (K. Karlsson et al., Biochem. J. 242, 1987, pp. 55-59). Although this heparin dosage is very high, a maximum

release was apparently not achieved. In the pig in which a maximal EC-SOD C release could be obtained with a very high heparin dose, 200 IU heparin per kg body weight resulted in a 50% of that maximal EC-SOD C release (K. Karlsson et al., *Biochim. Biophys. Acta* 967, 1988, pp. 110-114). Assumption of a similar dose-response relationship in man results in an estimate of total EC-SOD of about 66 U/ml plasma ( $20+2 \times 23$  U/ml). The total plasma volume is about 4.7% of the body weight corresponding to about 3.3 l in a 70 kg person. 1 unit EC-SOD equals about 8.8 ng. The total amount of EC-SOD in the blood vessels (plasma and vessel endothelium) is therefore  $3,300 \times 66 \times 8.8 \times 10^{-9}$  g = 1.92 mg. A tenfold increase would require 19 mg and a 300-fold increase 575 mg EC-SOD C. A suitable dosage of polypeptide of the invention may therefore be in the range of about 15-600 mg/day, dependent, i.e. on the type and severity of the condition for which administration of EC-SOD is indicated. Injection of, for instance, 87 mg EC-SOD C (a 50-fold increase) would result in 26  $\mu$ g/ml in plasma (disregarding endothelium binding). This or even lower concentrations show strong protective properties in *in vitro* experiments (with CuZn SOD) (cf. A. Baret, I. Emerit, *Mutation Res.* 121, 1983, pp. 293-297; K. Grankvist, S. Marklund, J. O. Sehlin, I. B. Taljedal, *Biochem. J.* 182, 1979, pp. 17-25).

**BSPR:**

For topical treatment, far less of a polypeptide composition of the invention as described above would probably be needed. At present, 4-8 mg of CuZn SOD are administered intraarticularly once a week for the treatment of arthritis. EC-SOD which has a far higher molecular weight is likely to remain in the joint for a longer period of time. A similar treatment protocol or possibly somewhat lower doses will probably be appropriate.

**CLPR:**

5. The polypeptide of claim 1, wherein said polypeptide is bound by an antibody which binds human EC-SOD type C but does not bind human CuZnSOD.

**ORPL:**

Borders et al., "Identification of ARG-143 as the Essential Arginyl Residue in Yeast Cu,Zn Superoxide Dismutase by use of a Chromophoric Arginine Reagent", *Biochemical and Biophysical Research Communications*, 96(3): 1071-1078, 1980.

**ORPL:**

Sieffens et al., "The Primary Structure of Cu,Zn Superoxide Dismutase from *Photobacterium leiognathi*: A likely case of gene transfer from eukaryotes to prokaryotes", *Hoppe-Seyler Z. Physiol. Chem.* 364: 675-690 (1983).

**ORPL:**

Steinman, Howard M., "The Amino Acid Sequence of Copper-Zinc Superoxide Dismutase from Bakers' Yeast", *The Journal of Biological Chemistry*, 255(14): 6758-6765, 1980.

**ORPL:**

Hering et al., "The Primary Structure of Porcine Cu-Zn Superoxide Dismutase", *Biol. Chem.*, 366: 435-445, 1985.

**ORPL:**

Lerch et al., "Amino Acid Sequence of Copper-Zinc Superoxide Dismutase from Horse Liver", *The Journal of Biological Chemistry*, 256(22): 11545-11551, 1982.

**ORPL:**

Tainer et al., "Determination and Analysis of the 2 A Structure of Copper, Zinc Superoxide Dismutase", *J. Mol. Biol.*, 160: 181-217, 1982.

**ORPL:**

Birmingham-McDonogh et al., "Reduced anion-affinity of Cu,Zn Superoxide Dismutases chemically modified at arginine", *Biochemical and Biophysical Research Communication*, 108(4): 1376-1382, 1982.

**ORPL:**

Borders et al., "Essential Arginyl Residues in Cu,Zn Superoxide Dismutase from

Saccharomyces Cervisiae", Carlsberg Res. Commun., 45 : 185-194, 1980.

ORPL:

Getzoff et al., "Electrostatic recognition between superoxide and copper, zinc superoxide dismutase", Nature, 306: 287-290, 1983.

ORPL:

Tainer et al., "Structure and mechanism of copper, zinc superoxide dismutase", Nature, 306: 284-286, 1983.

ORPL:

Borders et al., "Essentiality of the active-site arginine residue for the normal catalytic activity of Cu,Zn superoxide dismutase", Biochem. J., 230: 771-776, 1985.

ORPL:

Parge et al., "Crystallographic Characterization of Recombinant Human CuZN Superoxide Dismutase", The Journal of Biological Chemistry , 261(34) : 16215-16218, 1986.

ORPL:

Beyer et al., "Examination of the Role of Arginine-143 in the Human Copper and Zinc Superoxide Dismutase by Site-specific Mutagenesis", The Journal of Biological Chemistry, 262(23) : 11182-11187, 1987.

ORPL:

Sieffens et al., "The Primary Structure of Cu-Zn Superoxide Dismutase from Photobacterium leiognathi", Evidence for a Separate Evolution of Cu-Zn Superoxide Dismutase in Bacteria, Physiol. Chem. , pp. 675-690, Jun. 1983.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KOMC](#) | [Drawn Desc](#) | [Image](#)

---

5. Document ID: US 5223409 A

L23: Entry 5 of 5

File: USPT

Jun 29, 1993

US-PAT-NO: 5223409

DOCUMENT-IDENTIFIER: US 5223409 A

TITLE: Directed evolution of novel binding proteins

DATE-ISSUED: June 29, 1993

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ladner; Robert C.	Ijamsville	MD		
Guterman; Sonia K.	Belmont	MA		
Roberts; Bruce L.	Milford	MA		
Markland; William	Milford	MA		
Ley; Arthur C.	Newton	MA		
Kent; Rachel B.	Boxborough	MA		

US-CL-CURRENT: 435/69.7, 435/252.3, 435/320.1, 435/472, 435/5, 435/69.1,  
530/387.3, 530/387.5

ABSTRACT:

In order to obtain a novel binding protein against a chosen target, DNA molecules, each encoding a protein comprising one of a family of similar potential binding domains and a structural signal calling for the display of the protein on the outer surface of a chosen bacterial cell, bacterial spore or phage (genetic package) are introduced into a genetic package. The protein is expressed and the potential binding domain is displayed on the outer surface of the package. The cells or viruses bearing the binding domains which recognize the target molecule are isolated and amplified. The successful binding domains are then characterized. One or more of these successful binding domains is used as a model for the design of a new family of potential binding domains, and the process is repeated until a novel binding domain having a desired affinity for the target molecule is obtained. In one embodiment, the first family of potential binding domains is related to bovine pancreatic trypsin inhibitor, the genetic package is M13 phage, and the protein includes the outer surface transport signal of the M13 gene III protein.

66 Claims, 16 Drawing figures Exemplary Claim Number: 1

Number of Drawing Sheets: 16

L23: Entry 5 of 5

File: USPT

Jun 29, 1993

DOCUMENT-IDENTIFIER: US 5223409 A  
 TITLE: Directed evolution of novel binding proteins

## DEPU:

DOUG84: Dougan, G., and P Morrissey, "Molecular analysis of the virulence determinants of enterotoxigenic Escherichia coli isolated from domestic animals: applications for vaccine development", Vet Microbiol (1984/5), 10:241-57.

## DETL:

1) (CYS).sub.4 :Fe Rubredoxin (in CREI84, P. 376) 2) (CYS).sub.4 :Zn Aspartate Transcarbamylase (in CREI84, P. 376) and Zn-fingers (HARD90) 3) (HIS).sub.2 (MET)(CYS):Cu Azurin (in CREI84, P. 376) and Basic "Blue" Cu Cucumber protein (GUSS88) 4) (HIS).sub.4 :Cu CuZn superoxide dismutase 5) (CYS).sub.4 :(Fe.sub.4 S.sub.4) Ferredoxin (in CREI84, P. 376) 6) (CYS).sub.2 (HIS).sub.2 :Zn Zinc-fingers (GIBS88) 7) (CYS).sub.3 (HIS):Zn Zinc-fingers (GAUS87, GIBS88)

## ORPL:

CLEM90: Clements, John D. "Construction of a nontoxic fusion peptide for immunization against Escherichia coli strains that produce heat-labile and heat-stable enterotoxins", Infection and Immunity (1990), 58(5):1159-66.

## ORPL:

DOUG84: Dougan, G., and P. Morrissey, "Molecular analysis of the virulence determinants of enterotoxigenic Escherichia coli isolated from domestic animals: applications for vaccine development", Vet Microbiol (1984/5), 10:241-57.

## ORPL:

HOUG85: Houghten, et al. "A completely synthetic toxoid vaccine containing Escherichia coli heat-stable toxin and antigenic determinants of the heatlabile toxin B subunit", Infection and Immunity (1985), 48(3):735-740.

## ORPL:

WUJY89: Wu, et al. "Expression of immunogenic epitopes of hepatitis B surface antigen with hybrid flagellin proteins by a vaccine strain of Salmonella", PNAS (1989), 86:4726-30.

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#)

[KMD](#) | [Draw Desc](#) | [Image](#)

[Generate Collection](#)

Term	Documents
(21 NOT (9 OR 14 OR 6)).USPT,PGPB.	5

[Display](#)  Documents, starting with Document:

**Display Format:**  [Change Format](#)